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INDEX

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ACTA PÆDIATRICA

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Acta Pædiatrica **42**: 393—397. Sept. 1953

(From the Samariten Children's Hospital, Stockholm. Head: Prof. NILS MALMBERG)

Hyaluronidase in the Urographic Examination of Children

by HERMAN GLADNIKOFF and ERIK JACOBSSON

Hyaluronidase has proved to be of practical value as a "spreading factor." In the pediatric field, SCHWARTZMAN and his co-workers in New York have carried out valuable pioneering work along these lines. In Sweden, the substance has been studied by, among others, HALLÉN, in infusions and anesthetic investigations, and ALWALL in subcutaneous infusion tests.

As long ago as 1931 and 1938, respectively, BUTZEN-GEIGER and HUNT and POMPA tried the effect of a subcutaneous or intramuscular injection of opaque solutions in low concentrations in urographic examinations, but the injection of such large amounts of fluid caused much pain, absorption took place too slowly and the subsequent concentration of dye in the urine was usually too low. Since that time, opaque mediums causing no tissue damage even when used in fairly high concentrations (e.g. Umbradil) have become available, and in addition to this we are now able to hasten the absorption, and consequently the secretion, by using hyaluronidase. The method of injecting hyaluronidase followed by an intramuscular injection of opaque medium, was recommended by SIMON and NARINS and almost at the same time by OLSSON and LÖFGREN. It nearly always gave satisfactory urograms.

OLSSON and LÖFGREN injected first 2.5 viscosity reduction units (VRU) of hyalas intramuscularly and ten minutes later, a 10 per cent solution of contrast medium at the same site. In order to simplify the technique of urographic examinations and to avoid the often difficult intravenous administration of the opaque medium in infants, intramuscular injection of the medium was performed in addition to injection of hyaluronidase. With a view to obtaining a higher concentration of dye in the urine, lessening the pain caused by the injection and reducing the examination time, we have made a slight modification in this technique, by shortening the interval between the two injections. We have experimented along the following lines.

An amount of 2 $^1/_2$ VRU of hyaluronidase (the Hyalas "Leo" preparation was used in the majority of cases) was dissolved in $^1/_2$—1 ml of 0.5 per cent xylocaine (Astra) without adrenalin. This was injected into one of the buttocks. The needle was al-

lowed to remain in the muscle until the 35 per cent Umbradil solution was injected. Three minutes should elapse before this injection is carried out. The point of the needle must be held at exactly the same depth for both injections. The same amount of contrast medium per kg of body weight as is used in intravenous injections is usually sufficient. The concentration of dye in the urine will be higher if hyaluronidase had not been used but lower than after an intravenous injection of the same amount of contrast. It is sufficiently high, except in the case of infants under 1 $^1/_2$ years of age or if there is a large quantity of gas in the abdomen. In the latter cases, the amount of opaque medium per kg of body weight can be doubled. This is especially advisable in young infants. The roentgen examination is then carried out in the usual way.

As in the case of intravenous injections of contrast medium, the concentration of opaque substance is often inadequate in infants under six months and in children with a lowered concentration capacity due to extensive damage in the renal parenchyma.

We observed no ill-effects either locally or generally. We did not have an opportunity to study tissue specimens from the injection site, but Umbradil in 35, 50 and 70 per cent solutions is used in both adults and children in vasographic examinations. Much larger quantities than those in question often accumulate around the vessels in these examinations without causing any tissue damage other than transient swelling and tenderness. Nor have we observed any side-effects due to the xylocaine or hyaluronidase.

Our technique was gradually worked out by injecting into one of the buttocks first 2 $^1/_2$ VRU of hyaluronidase in a xylocaine solution and then the opaque medium. Into the other buttock we injected at the same time, for purposes of comparison, either contrast medium alone or varying amounts of hyalas followed by contrast medium. Differences in the spread, absorption and secretion of the opaque substance in the urine could be ascertained from the roentgen pictures (see Fig. 1 and 2). The method, though rough, is adequate for the purpose. In a similar manner, we arrived at a suitable interval between the two injections, and so on.

Only a very small amount of hyaluronidase is required. We could observe no difference in the spread of the opaque medium through the muscles, its absorption away from that area or its concentration in the urinary passages, when 2 $^1/_2$ VRU were injected and when $^1/_{16}$th of a VRU was the amount chosen. The concentration of opaque substance in the urine was noticeably improved when hyalas was used; this is particularly helpful when there is gas in the intestine. Adequate concentration can, however, also be obtained in many instances when opaque medium is injected intramuscularly without hyalas.

An interval of about 3 minutes should elapse between the injection of hyaluronidase and of radiopaque medium. Prolongation of the interval beyond this time produced no appreciable improvement in the spread, absorption

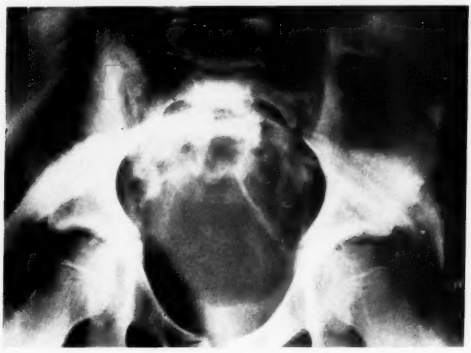

Fig. 1. Intramuscular spreading of contrast medium 4 minutes after injection. The opaque medium spreads more rapidly with preliminary treatment with hyalas (H) than without.

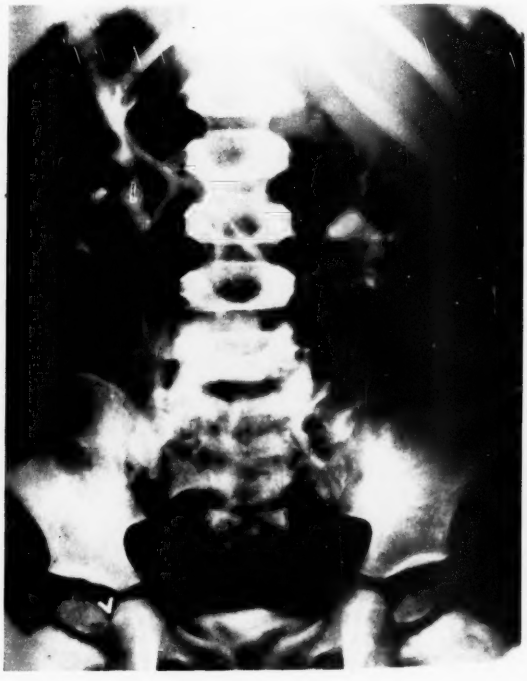

Fig. '. Intramuscular injection of radiopaque medium using the author's technique, gives good contrast concentration.

or secretion of the opaque substance. On the other hand, the spreading effect does not reach its height with an interval of less than 3 minutes.

Xylocaine does not hinder the spreading effect of hyaluronidase. The local anesthesia so completely eliminates the pain and sense of tension usually produced by the injection of the contrast medium that the child does not notice when this is being carried out, provided its attention is suitably distracted.

No definite reports have been published regarding sensibilization with hyaluronidase, but some investigators have suggested that an injection of this drug might produce some form of "antihyaluronidase." An antibody of this kind could impede or suspend the spreading effect exercised by hyaluronidase on the radiopaque medium, when repeated roentgen examinations are carried out. We had an opportunity, in three cases, to repeat a urographic examination with an intramuscular injection of contrast medium. Half the dose was injected in the usual manner, in conjunction with hyaluronidase, on one side, and half the dose without preparatory treatment with hyaluronidase on the other side. The hyaluronidase hastened the spread, absorption and excretion as usual. In other words, these cases yielded nothing to corroborate the theory as to the formation of antihyaluronidase. The renewed examinations were carried out after an interval of 2—3 months.

Intramuscular injection of contrast medium still naturally remains the method of choice in those cases where readily accessible superficial veins are available.

Summary

A method for the urographic examination of children, especially those in the early years of life, is described. Treatment of the injection site with hyalas (Leo), dissolved in 0.5 per cent xylocaine (Astra), prepared the area so satisfactorily that the subsequent injection of contrast medium caused little pain and the resistance offered to the injection was lessened. The spread, absorption and consequently also the excretion of the dye were thus accelerated. A satisfactory concentration of dye in the ureters was thus obtained.

Hyaluronidase au cours des examens urographiques.

Les auteurs décrivent une méthode d'urographie chez l'enfant et spécialement lors des premières années de la vie. L'injection préalable de hyaluronidase (Leo), dissoute dans la xylocaine (Astra) à 0,5 %, prépare la région si bien que l'injection de substance-contraste ne donne aucune peine et que la résistance offerte à l'injection est diminuée. L'importance de l'absorption et, en conséquence, également celle de l'excrétion du contraste sont ainsi accélérée. Une concentration satisfaisante de ce dernier dans les uretères est obtenue.

Hyaluronidase bei der urographischen Untersuchung.

Eine Methode zur urographischen Untersuchung von Kindern, besonders in den frühen Lebensabschnitten, wird beschrieben. Die Behandlung der Injektionsstelle

mit Hyalas (Leo), gelöst in 0,5 Prozent Xylocain (Astra), bereitet die Stelle so ausreichend vor, dass die nachfolgende Kontrastmittelinjektion wenig Schmerzen verursacht und der Widerstand gegenüber der Injektion geringer wird. Ausbreitung, Absorption und schliesslich auch Ausscheidung des Kontrastmittels werden dadurch beschleunigt. Eine zufriedenstellende Konzentration des Kontrastmittels in den Ureteren wird damit erreicht.

Hialurodinasa en el examen urográfico de los niños.

Se describe un método para el examen urográfico en niños, especialmente durante los primeros años de la vida. El tratamiento del sitio de la inyección con hialasa (Leo), disuelta en un 0,5 por ciento de xilocaina (Astra), lo prepara tan satisfactoriamente que la inyección subsiguiente de medio de contraste solo causa pequeñas moletias y la resistencia ofrecida a la inyección fué pequeña. La divulgación, absorción y en consecuencia también la excreción del medio de contraste fueron acceleradas. De este modo se obtuvo una concentración satisfactoria del medio de contraste en los ureteres.

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Late Prognosis in Asphyxia Neonatorum

by B. HELLSTRÖM and B. JONSSON

The results obtained from earlier investigations on the prognosis in asphyxia neonatorum have revealed marked discrepancies, which were mainly due to variations in the composition of the materials. This may be attributed to the difficulty in obtaining a uniform primary material. In the present paper, an attempt is made to correlate the late prognosis with various symptoms during the newborn period, using cases treated and observed for asphyxia neonatorum at Norrtull's Hospital and later subjecting them to a follow-up examination.

Previous investigations were carried out in two different ways. One of the methods is retrospective, and is based on a material comprising mentally and neurologically defective children. It showed the extent of neonatal asphyxia in these cases. In the other method, the material consists of children with neonatal asphyxia who were later submitted to a follow-up examination after a few years. This provides a better conception of the prognosis.

SCHREIBER's investigation is an example of the former type. In a material of 900 spastic children and children suffering from convulsive diseases, a history of asphyxia was noted in 70 per cent, regardless of the manner of delivery or whether the baby was born at full term, or was premature or a twin. BELNAP *et al.* studied a series of cases in order to try to determine the incidence of birth injury as a cause of late cerebral disorders. They found evidence that birth injury may be a major factor in their causation. Viewed in retrospect, however, no distinction is made from this evidence, between cerebral birth injury due to anoxia and that due to direct trauma. The subsequent behaviour was affected by prenatal, natal and postnatal anoxia, as concluded from investigations performed by PRESTON and ROSENFELD and BRADLEY.

Among the second group i.e. material subjected to a follow-up examination, the work by HANNES may be mentioned. He was unable to find any correlation between asphyxia and a subsequent mental retardation or Little's disease. Still, the primary mortality was considerable (viz. 42 per cent). MC PHAIL and HALL did not report any proof of mental retardation in children who were apneic

at birth. The group of severe apnea included children who developed cyanosis in the first few days of life. Nor were CAMPBELL *et al.* able to see any difference in the physical or mental development between children who were asphyctic at birth and a control group. Neurological lesions including convulsions were not more frequent among children who were asphyctic at birth, as observed by KEITH and NORVEL. WETTERDAL reported an extensive material of forceps delivery, in which asphyxia was the main indication for forceps. Thus, the diagosis in these instances was prenatal. The asphyxia group showed a greater primary mortality rate, but the asphyxia did not cause any increase in the number of physically or mentally injured children in the surviving cases. USDIN and WEIL, in a material subjected to statistical analysis, recently were unable to establish any difference in the intelligence quotient of children apneic at birth and a control group. However, all the children were excluded from the material who had any abnormal neurological findings at the time of birth, during the neonatal period or at the time of the present investigation. DARKE arrived at a result, different from those of the forementioned authors, noting a statistically significant lowering of the intelligence quotient in a group of children asphyctic at birth. The author's criteria on so-called asphyxia are more strict than those of other investigators, and he included only children with so-called asphyxia pallida or those who were apneic for more than 3 minutes. Cases with positive neurological findings at the time of birth, during the neonatal period or at the time of the follow-up examination were excluded, as well as those with diagnosed or suspected intracranial haemorrhage. The author admit that it is a difficult problem to exclude cases of intracranial haemorrhage.

Own investigations

The material comprises children who were admitted as newborns to the Norrtull Children's Hospital from maternity hospitals during the years 1943—1949. The children were reported to have been asphyctic at birth, or, to have manifested signs of deficient oxygenation during the first days of life, or were suspected to have a cerebral injury (attacks of cyanosis, convulsions). Children with a birth weight below 2500 g were excluded, as well as those who revealed non-cerebral organic diseases (organic congenital heart disease, malformations in the digestive tract, etc.) at a later observation at the hospital. Eightyfive children conformed to the requirements. Symptoms were noted from the hospital records which might suggest a cerebral lesion, and their duration stated. These symptoms were cyanosis, need of extra warmth, tube-feeding, vomiting fits, convulsions, changed tonus and bulging fontanel.

Eighteen of the 85 cases included in the material died in hospital in the newborn period. All were subjected to autopsy. Four of the remaining 67 died later, all at hospitals where they were subjected to autopsy. They died at the respective ages of 1, 2, 2, and $6^1/_2$ years. In 61 of the 63 survivals, reliable and up to date information could be obtained. The two remaining cases had left the country. One of the latter

was examined at the age of six months at a children's outpatient's department but as this examination dates rather far back and was performed when the patient was very young, the case was not considered to have been satisfactorily followed up. Thus, the total number of traced cases, including the deaths, is 65. Among the 61 survivals, the present authors examined 53, the rest being examined at other hospitals. At the follow-up examination, the children were between 2 and 9 years. After an anamnesis in which the parents were interrogated as to the physical and mental development of their child, behaviour disorders, school reports, social adaptability, occurrence of convulsions, cerebral trauma, encephalitis, etc., a full neurological examination was performed, and in most cases supplemented by tests e.g. Terman-Merril on children over 3 years of age and development tests acc. to Bühler-Hetzer on children under 3. These tests were carried out by the same psychologist (Miss Ulla Östrand) in the homes of the children. In a few instances, a brother or sister was tested for comparison. An electroencephalographic examination was performed (published in this issue by M. D'AVIGNON and H. KEILSON).

Results

The 18 deaths in the newborn period are reported in Table 1. Intracranial haemorrhage occurred in a remarkably large number of cases. However, this cannot always be accepted as the cause of the death. An anoxic cerebral necrosis is more difficult to ascertain patho-anatomically, particularly in the case of death during the first days of life. One child died in the first day of life, 11 on the second, 2 on the fourth and the rest on the tenth, thirteenth, and seventeenth days of life, respectively. Cyanosis and decreased tonus were common symptoms, while convulsions and bulging fontanels were not so frequent as might have been expected.

TABLE 1

Deaths during newborn period	18
Intracranial haemorrhage	15
Clinical symptoms:	
Cyanosis	15
Convulsions	6
Decreased tonus	10
Increased tonus	2
Bulging fontanel	3

Eighteen of the 65 children subjected to follow-up examination disclosed disturbances that may be attributed to paranatal cerebral injuries (Table 2). These disturbances consisted of spasticity, convulsions and mental retardation (development and intelligence quotient below 80). Four of these died as previously stated, and reliable data regarding the clinical picture were obtained.

In Figures 1—4 and Table 3, the symptoms during the newborn period were correlated to the number of children manifesting defects at the follow-up

TABLE 2

Children found defective at follow-up examination.

Spasticity	3
Convulsions	3
Oligophrenia	6
Spasticity + Oligophrenia	2
Spasticity + Oligophrenia + Convulsions	3
Convulsions + Oligophrenia	1
Total number of children	18

examination. No increase in the frequency of defective children seems to have occurred among those who were cyanotic in the newborn period as compared to those with no noted cyanosis (Fig. 1, Table 3). An inability to regulate the body temperature in full term children is considered to be a cerebral symptom. However, in the group requiring extra warmth, the frequency of defective children is not particularly high (Table 3), nor does any notable connection exist between the so-called functional vomiting fits in the newborn period and the cerebral injuries (Table 3). The absence of a normal sucking reflex in full term newborns is more often observed in the cases with cerebral injury. These children had to be fed by tube and in this group defective

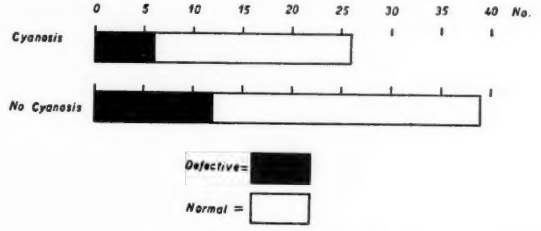

Fig. 1. Number of defective and normal cases at the follow-up study, among children cyanotic and not-cyanotic at birth.

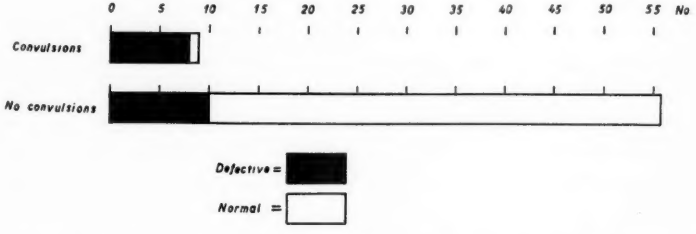

Fig. 2. Number of defective and normal cases at the follow-up study, among children with convulsions and no convulsions at birth.

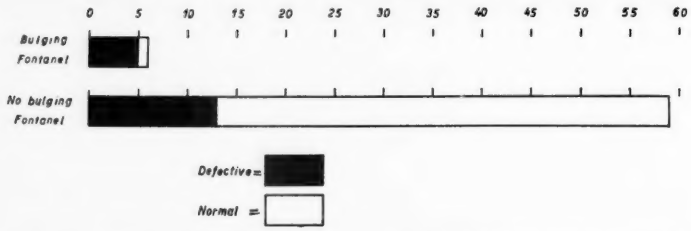

Fig. 3. Number of defective and normal cases at the follow-up study, among children with bulging fontanel and no bulging fontanel at birth.

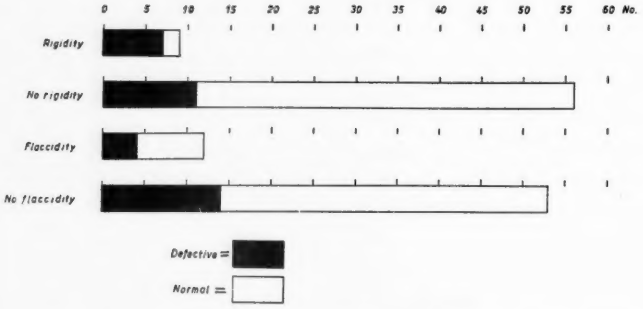

Fig. 4. Number of defective and normal cases at the follow-up study, among children with change of tone and no change of tone at birth.

children are twice as frequent as in the group not fed by tube (Table 3). When tube-feeding had to be continued up to or even beyond the fifth day of life, the frequency became three times as great. The occurrence of convulsions in the newborn period, irrespective of whether they are manifestations of an intracranial haemorrhage or of an anoxic cerebral injury, is apparently a grave symptom with regard to the late prognosis (Fig. 2, Table 3). Eight of 9 children with convulsions in the newborn period were defective, 6 of them had repeated fits later in life. The frequency of defective children will be seen to be five times as great in the group with convulsions in the newborn period as in the group without neonatal convulsions. There is also a notable connection between the occurrence of a bulging fontanel and a poor late prognosis, viz. 5 of 6 children with bulging fontanels became defective, which is four times as common as in the group with no bulging fontanel (Fig. 3, Table 3). The changed tonus seems to be an important symptom in this connection (Fig. 4, Table 3), especially an increased tonus. This yields a frequency of defective children four times as great as children lacking these symptoms, and five times greater when combined with convulsions.

TABLE 3

Relation between frequencies of defective children (spastics, convulsions, intellectually retarded) with and without the respective symptoms during the newborn period.

Cyanosis	0.7
Need of extra heat supply up to 5—15 day of life	1.1
Need of extra heat supply later than fifteenth day of life	1.3
Vomiting fits	1.4
Vomiting fits later than fifth day of life	1.5
Tube-feeding required	2.0
Tube-feeding required later than fifth day of life	3.0
Convulsions	4.9
Increased tonus	3.9
Decreased tonus	1.3
Bulging fontanel	3.8

As the material is relatively small and the number of children in the groups with and without the respective symptoms varies, these figures must be viewed with some reservation. Still, they give an indication of the particular symptoms that suggest a poor late prognosis. A comparison of the frequencies of defective children with and without the symptoms in the newborn period is made in Table 3.

Discussion

It is essential for an investigation on prognosis that the primary material is clearly defined. However, this is very difficult, since, in asphyxia neonatorum, one is not dealing with a uniform disease, but merely a clinical term or complex of symptoms with extremely varying causes. Asphyxia may be defined as anoxia with carbon dioxide retention due to disturbed ventilation or respiration, but it can be attributed to widely differing diseases in the air passages, the lung parenchyma, the pleura, the respiratory musculature or in the nervous regulating mechanism. The discrepancy in the results from different investigations on the late prognosis may no doubt be attributed, as previously stated, in the first place to variations in the composition of the materials. Often the investigation is limited to newborns who began to breathe later than 3 minutes after parturition, though this does not guarantee a homogeneous material. When this kind of investigation is performed at a hospital where narcotics are administered generously during delivery, the material will be dominated by cases due to narcotization of the child's respiratory centre. Should a similar investigation be performed at another hospital, perhaps cerebral injuries due to birth trauma would predominate.

The brain is the organ most susceptible to anoxia. Accordingly, the prognosis in asphyxia neonatorum is judged by paying special regard to the occur-

rence of cerebral injuries. Asphyxia due to narcotization of the respiratory centre or aspiration of amniotic fluid should yield a better prognosis than an asphyxia attributable to cerebral haemorrhage with injury to, inter alia, the nervous regulation of respiration. It would therefore be desirable to be able to exclude cases of cerebral haemorrhage, but this is unfortunately often impossible by means of clinical examination. Even at post mortem, it may be difficult to decide whether a cerebral haemorrhage was the cause of the asphyxia or a sequelae. Consequently, we have not tried to maintain this distinction. However, this fact makes the material more heterogeneous and it is an advantage when one considers that the purpose of the investigation was to correlate the prognosis with different symptoms during the newborn period.

In comparison with other investigations, the prognosis in this material is strikingly poor. Eighteen of 85 children died during the newborn period, and 18 of the 65 who survived and who were submitted to a follow-up examination manifested clinical signs of permanent cerebral injury. In contrast to this result, other investigations may be mentioned that started with cases showing apnea directly after parturition and later showed a normal development. This seems to be in good conformity with general clinical experience, viz. that asphyxia appearing later on and only after the child has breathed normally for a time has a less favourable prognosis. The foetus and the newborn possess a marked resistence to anoxia and the metabolism is relatively anaerobic. When, on the other hand, a readjustment to extrauterine life has already taken place, an anoxia will indicate something much more serious and give rise to much graver injuries. Another explanation may be that cerebral injury due to birth injury may more often show symptoms some time after parturition.

It is not surprising that cyanosis is irrelevant to the late prognosis. Cyanosis and anoxia are not strictly correlated to one another. The cyanosis is dependent on the content of reduced haemoglobin in the capillary blood. In this respect the total haemoglobin content is of great significance. Newborns with a high haemoglobin content may present cyanosis even with only a mild anoxia. On the other hand, it may be difficult to observe cyanosis in many instances with a severe anoxia when a simultaneous shock with pronounced pallor is present.

The cases manifesting convulsions, changed tonus, bulging fontanel and deficient sucking reflex during the newborn period, had a less favourable prognosis.

Summary

Eightyfive children treated at a children's hospital for asphyxia neonatorum were subjected to a follow-up examination. Eighteen died during the newborn period. Sixtyfive of the 67 survivals were followed up. Among them 18 showed signs of a permanent cerebral injury (spasticity, mental retardation, convulsions). The late prognosis was correlated to different clinical symptoms during the newborn period. Children with convulsions, changed tonus, bulging fontanel, reduced sucking capacity have a conspicuously bad prognosis.

Pronostic tardif de l'asphyxie néonatale.

85 enfants traités à l'hôpital d'enfants pour une asphyxie néonatale ont été soumis à un examen ultérieur. 18 moururent pendant la période néonatale. 65 des 67 survivants ont été suivis. Parmi ceux-ci 18 présentaient des signes de lésion cérébrale permanente (spasticité, retard intellectuel, convulsions). Le pronostic ultérieur était conditionné par les différents symptomes constatés pendant la période néonatale. Les enfants présentant des convulsions, des modifications du tonus, une fontanelle bombante, une diminution de la fonction de téter, eurent une évolution de mauvais pronostic.

Spätprognose bei Neugeborenenasphyxie.

85 Kinder, welche in einem Kinderhospital wegen Neugeborenenasphyxie behandelt worden waren, wurden einer katamnestischen Studie unterzogen. 18 starben während der Neugeborenenperiode. 65 von den 67 Überlebenden wurden nachuntersucht. Unter diesen zeigten 18 Zeichen eines cerebralen Dauerschadens (Spastizität, geistige Unterentwicklung, Krämpfe). Die Spätprognose wurde in Beziehung gesetzt zu verschiedenen klinischen Symptomen während der Neugeborenenperiode. Kinder mit Krämpfen, verändertem Tonus, vorgewölbter Fontanelle, verminderter Saugfähigkeit haben eine bedeutend schlechtere Prognose.

Pronóstico tardio en la asfixia neonatal.

Ochenta y un niños tratados en el hospital infantil por asfixia nenonatal fueron sometidos a un control seguido. 18 murieron durante el periodo del recien nacido. Se siguió el control de 65 de los 67 supervivientes. Entre ellos 18 mostraron síntomas de un menoscabo cerebral permanente (espasticidad, retardación mental, convulsiones). El pronóstico tardío estuvo en relación con diferentes síntomas clínicos durante el periodo del recien nacido. Niños con convulsiones, tono alterado, distensión de las fontanelas, capacidad de chupar reducida, tienen claramente un mal pronóstico.

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Electro-Encephalographic Findings in Children, Previously Treated for Asphyxia Neonatorum

by M. d'AVIGNON and I. KEILSON

In the present issue (Acta Pædiatrica 42: 398, 1953), B. JONSSON and B. HELLSTRÖM publish a paper on the late prognosis in asphyxia neonatorum, and they report their observations from a follow-up of 61 newborns treated for neonatal asphyxia. This foollw-up study also included electro-encephalographic examinations performed on 44 children, an account of which is given in this report.

The electro-encephalographic registrations were carried out with a 6-channel Grass apparatus. On each occasion, 10 silver electrodes were applied, to the frontal, parietal, temporal and occipital positions and, as reference electrodes, on the ears, unipolar and bipolar leads from all electrodes. The registrations were interpreted with no prior knowledge of the patient except the age. It was only after all the curves had been analysed that the results were compared to the data originating from the follow-up.

	Group 1	Group 2	Group 3
Cerebral palsy	2		
Epilepsy	3		
Microcephaly	1		
Behavior disorders	3		
1 Q 45–55			
1 Q 55–70	2		
1 Q 70–85	3		
1 Q 85–90		1	
1 Q 90–110		7	9
1 Q 110–120		3	4
1 Q 120–130		4	1
1 Q over 130		1	
Number of cases:	14	16	14

Table 1.

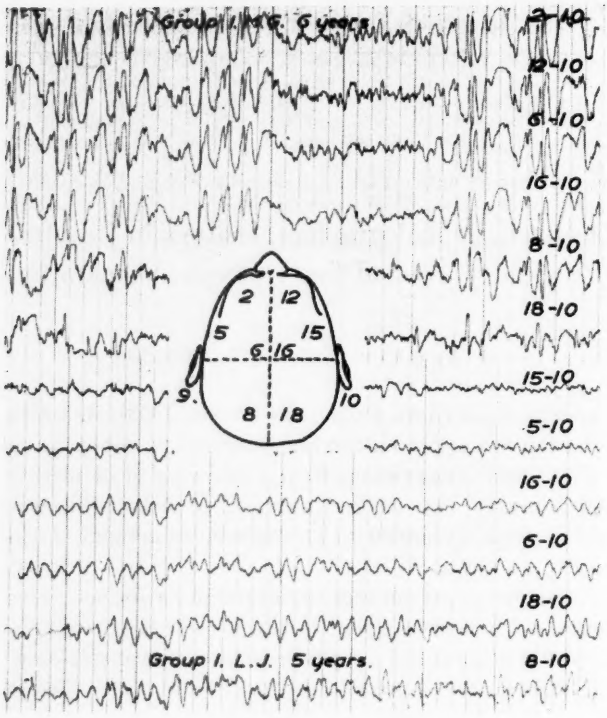

Fig. 1.

There is a lack of normal material in the electro-encephalographic literature. According to LENNOX, GIBBS and GIBBS, up to 10 per cent of electro-encephalograms obtained from adults may deviate from normal. When the material consists of selected healthy cases, only 5 per cent will be found to deviate from normal. According to WALTER, only 1 per cent of a "normal population" would display electro-encephalographic deviations from normal registrations. From a minor series of normal Swedish children (B. HOLMGREN), about 5 per cent were found to have electro-encephalograms deviating from normal.

The electro-encephalographic registrations were grouped as shown in Table 1.

Group 1: Pathologic electro-encephalograms with clearly pronounced dysrhythmia, numerous slow waves, hemispheric asymmetry, focal findings with pathologic wave complexes or a paroxysmal break-through of pathologic wave-complexes (Fig. 1).

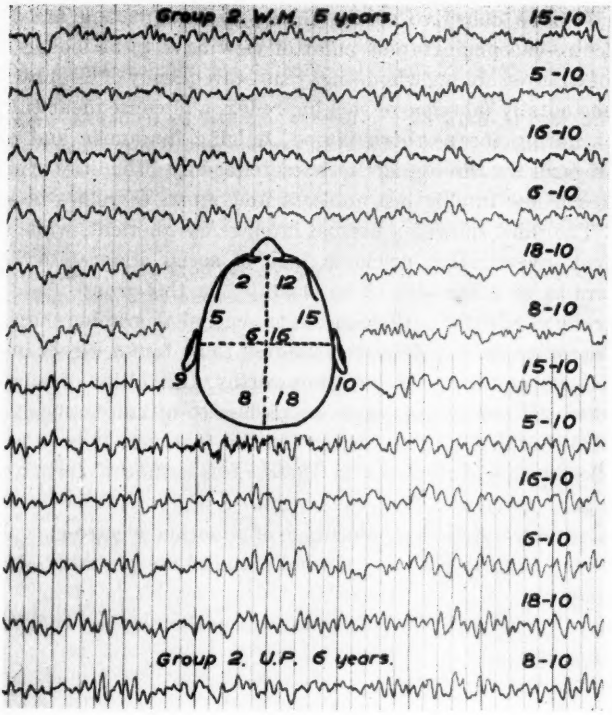

Fig. 2.

Group 2: Slightly pathologic electro-encephalograms, implying a slight dysrhythmia with sparse slow frequencies (Fig. 2).

Group 3: Normal electro-encephalograms.

Results

In Table 1 the results were brought together from the follow-up examination of cases with electro-encephalographic findings grouped as pathologic (1), slightly pathologic (2) and normal (3).

As far as Group 1 is concerned, we have succeeded in registering JONSSON's and HELLSTRÖM's 14 follow-up patients with findings of disturbances that may be connected with perinatal cerebral injuries. These disturbances include cerebral palsy, epilepsy, backwardness and a case of microcephaly. Thus the defective children are to be found among those with pathologic electro-encephalograms. When comparing these findings with the postnatal symptoms,

those found to be defective at the follow-up examination and pathologic from an electro-encephalographic point of view have to be looked for among the group of children among whom the greatest frequency of cerebral symptoms occurred postnatally (absence of sucking reflex, and consequent tube-feeding, convulsions during the newborn period, bulging fontanelle and changes of tonus). As regards the three children characterized by difficulties of adaptation, two revealed a low intelligence quotient and must, therefore be defined as defectives. The third showed a normal intelligence quotient, while the social-psychological investigation disclosed lack of social adaptability of such a grave nature as to cause him to be classified in this group.

In the group of slightly pathologic electro-encephalographic changes (Group 2), there are no longer any defective children to be found, either in a somatic or a mental respect. Nor are any noteworthy difficulties of adaptation to be found here. It would appear to be useless to attempt any explanations of the electro-encephalographic changes in this instance. It is to be supposed that the electro-encephalograms in these cases reflect a certain degree of cerebral injury, though not of such a nature or importance as to produce any clinical symptoms. Such a percentage of abnormal electro-encephalograms as are expected to form part of a normal material are probably also included in this group.

Finally, as to Group 3, the patients as well as their electro-encephalograms, are normal.

Summary

At follow-up examination of 61 children subjected to postnatal treatment for asphyxia neonatorum in the newborn period, 44 disclosed electro-encephalographic changes. Grave pathologic findings were only noted in children who, at the follow-up, showed somatic and mental defects (14), while children with slight electro-encephalographic changes (16) have developed well in all respects up to the age at which the follow-up were performed, in spite of a neonatal asphyxia. The neonatal asphyxia in these cases is supposed to have produced organic cerebral injuries of such a degree or nature as to disclose no clinical, but simply electro-encephalographic, changes.

Recherches électro-encéphalographiques chez les enfants traités anteriuerement pour l'asphyxie néonatale.

L'examen de 61 enfants soumis à un traitement contre l'asphyxie néonatale après la naissance, montra que 44 de ceux-ci présentaient des modifications électro-encéphalographiques. De grâves modifications ne furent seulement notées que chez ceux qui présentèrent des troubles somatiques ou mentaux ultérieurs (14), tandis que les porteurs de tracés peu troublés présentèrent un developpement normal pour l'âge (16) en dépis d'une asphyxie néonatale. Cette dernière peut être tenue comme responsable de lésions cérébrales n'entrainant pas de signe clinique mais seulement des modifications du tracé électro-enceéphalographique.

Elektroencephalogrammbefunde bei Kindern, welche früher wegen Neugeborenenasphyxie behandelt worden waren.

Bei einer Nachuntersuchung von 61, wegen postnataler Asphyxie in der Neugeborenenperiode behandelter Kinder, ergaben 44 elektroencephalographische Veränderungen. Schwere pathologische Befunde wurden nur bei Kindern festgestellt, die bei der Nachuntersuchung somatische und geistige Defekte (14) zeigten, während Kinder mit leichten electro-encephalographischen Veränderungen (16) sich in jeder Hinsicht altersgemäss bis zum Zeitpunkt der Nachuntersuchung — trotz der Neugeborenenasphyxie — entwickelt haben. Es wird angenommen, dass die Neugeborenenasphyxien in diesen Fällen zu organischen Gehirnschädigungen von solchem Grad und solcher Natur geführt haben, dass wohl keine klinischen, aber einfache elektroencephalographische Veränderungen zustandekommen.

Hallasgos encefalográficos en niños, previamente tratados por asfixia neonatorum.

De 61 niños tratados por asfixia neonatorum en el período de recién nacidos, 44 mostraron cambios encefalográficos. Graves hallasgos patológicos solo fueron notados en chicos que luego mostraron defectos somáticos y mentales (14), mientras que los niños con pequeños cambios encefalográficos (16) se desarrollaron bien en todos los aspectos hasta la edad en que fueron seguidos, apesar de la asfixia neonatal. Se supone que la asfixia neonatal en estos casos produjo injurias orgánicas en el cerebro de tal grado o naturaleza que sin dar signos clínicos, producían simples cambios electroencefalográficos.

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From the Pediatric Clinic of Karolinska Sjukhuset, Stockholm (Chief: Professor A. Wallgren) and the State Chemico-Legal Laboratory, Rh-department (Chief: Docent B. Broman)

Experiments with a New Agglutination Method for Ascertaining Antibodies in Allergic Subjects

by SVEN KRAEPELIEN, BENGT SIEVERT and STEN WETTERGREN

P. KALLÓS and L. KALLÓS-DEFFNER, in Volume 2 of the International Archives of Allergy and Applied Immunology, give a preliminary report of a method by which they were able to ascertain antibodies to different types of allergens in sera taken from allergic subjects. The authors, however, point out that it has not yet been possible, by serological methods, to trace the different types of antibodies present in allergic subjects which have to be considered (bivalent and monovalent), although this has been performed by a serological technique in experimentally sensitized animals. Accordingly, by using serum from sensitized animals collodium particles have become agglutinated upon which the allergen in question has been adsorbed. This Jones-Cannon-Cavelti test is far more sensitive than other serological methods which have been used but, nevertheless, has failed to give any encouraging results in tests with human-allergic sera.

However, the two investigators tried the method and, in a few instances, found direct agglutination of the particles with sera from human allergic subjects. When the results were negative, they assumed that a binding of antibodies to the allergen at the particle surface could, nevertheless, have taken place. These antibodies should in that case be monovalent, and not agglutinating. The authors, therefore, after bringing the allergen-coated particles into contact with the specific antiserum, tested them according to the Coombs' method which gave a further number of posititve reactions in support of their assumption. Still, several negative reactions remained, which they attributed to defects in the collodium particles, inter alia, in regard to the adsorption capacity.

In trying to find other corpuscular elements with a better allergen-adsorption, they tested erythrocytes according to the method presented by MIDDLE-

BROOK and DUBOS for ascertaining antibodies to tubercle bacilli, by means of tuberculin-treated blood corpuscles of sheep. The capacity of the blood corpuscles of sheep to adsorb the particular allergens concerned here (pollen, flour) proved however to be slight. Their capacity could, nevertheless, be considerably increased by previous treatment with Forsman antiserum in subliminal concentration, i.e. at a dilution just above that barely producing agglutination of the blood corpuscles.

When these previously treated blood corpuscles had adsorbed allergens, they were tested against sera from patients who had proved hypersensitive to corresponding allergens. This caused a specific, direct agglutination in the great majority of the cases. The negative tests could, moreover, be further reduced by using Coombs' method. However, the material was small.

P. KALLÓS and L. KALLÓS-DEFFNER, in a second experimental series, substituted human O-blood corpuscles for the blood corpuscles of sheep. This is undoubtedly an advantage in an investigation of human sera of this kind. By applying homologous blood corpuscles, the significance of hetero-antibodies in human sera directed straight at the animal blood corpuscle is eliminated. The allergen-binding capacity of the O-blood corpuscles should in this case be achieved by treatment with a subliminal concentration of anti-H-serum from eel. This method is stated to have shown promising results in spite of the still small experimental series employed.

Own investigations

Our own investigations were aimed at the latter alternative. Our material comprised sera from 14 children and 25 adults, selected as far as possible from monovalent allergic subjects with a pronounced allergy. Some of these patients, however, at the intradermal test (and partly also at exposure tests) reacted to several antigens. Accordingly, serum from those cases was, in a few instances, tested against a couple of antigens. Fifty-one test swere performed with these 39 human sera (4 of which were double tests) against the following allergens:

Pollen of birch	15 cases
Pollen of timothy grass	26 cases
Horse epithelium	3 cases
House dust	3 cases.

With regard to the technical details, similarly to P. KALLÓS and L. KALLÓS-DEFFNER, we used Smith's and Scott's modification of Middlebrook's and Dubos' method for ascertaining antibodies against tubercle bacilli. Our method was as follows:

The eel serum employed was found to be reliable at a subliminal concentration in a dilution of 1/800 against O-blood corpuscles (microscopic agglutination in dilution 1/512).

To this eel serum dilution was added a mash of washed human O-blood corpuscles up to a 2 % suspension which was incubated for 4—6 hours at +4° C (the optimal temperature for anti-H-effect). Then the blood corpuscles were separated from the eel serum by slow centrifugation, washed once and resuspended up to 2 % in Eagel's solution. Equal parts of this suspension and a 10 % allergen solution were then incubated, being mixed every quarter of an hour, for one hour at 37° C. After depositing this suspension at +4° C overnight, centrifugation, washing and resuspension were performed as before.

To 0.5 cc of this 2 % suspension of the eel serum and the allergen-treated blood corpuscles, 0.5 cc of serum was added from a patient with an allergy to the corresponding allergen. This mixture was also incubated, whilst mixed every quarter of an hour, for an hour at 37° C. Macro- and microscopic readings were made after the sample had been kept overnight at +4° C.

No direct agglutination was observed in any of the 51 tests. All the suspensions were also tested after three washings in physiological saline with Coombs' serum on a slide. No agglutination of the blood corpuscles was observed after this treatment in any single case.

Thus, this experimental series provides no evidence of the possibility of successfully using human O-blood corpuscles as allergen-carrying corpuscles for ascertaining antibodies in allergic subjects.

Summary

The authors subjected a method, presented by P. KALLÓS and L. KALLÓS-DEFFNER, for ascertaining specific antibodies in allergic subjects by applying human O-blood corpuscles as allergen-carrying corpuscles, to a control test. In an investigation series (39 cases), no positive results were obtained either in direct agglutination tests or by Coombs' technique.

Recherches pour mettre en évidence la présence d'anticorps chez les sujets allergiques à l'aide d'une nouvelle méthode d'agglutination.

Les auteurs donnent leur avis sur une méthode présentée par P. KALLÓS et L. KALLÓS-DEFFNER destinée à affirmer la présence d'anticorps chez les allergiques en application du principe qui veut que les corpuscules O du sang humain sont les corpuscules vecteurs de l'allergie et peuvent être soumis à un test de contrôle. Dans une étude de 39 cas, ils n'obtinrent aucun résultat positif soit par les tests d'agglutination directe, soit grâce à la technique de Coombs.

Versuche mit einer neuen Agglutinationsmethode zur Festellung von Antikörpern bei allergischen Personen.

Die Autoren unterwarfen eine von P. KALLÓS und L. KALLÓS-DEFFNER angegebene Methode einer Kontrolle. Dabei werden spezifische Antikörper bei allergischen Personen durch Zufuhr menschlicher O-Blutkörperchen als allergentragenden Körpern nach-

gewiesen. In einer Untersuchungsreihe (39 Fälle) wurden weder beim direkten Agglutinationstest noch mittels der Coombs-Technik positive Resultate erhalten.

Investigaciones con un nuevo método de aglutinación para la determinación de anticuerpos en sujetos normales.

Los autores exponen un método como test de control, presentado por P. KALLÓS y L. KALLÓS-DEFFNER, para determinar anticuerpos específicos en sujetos alérgicos aplicando glóbulos humanos de sangre O como corpúsculos portadores de alergeno. En una serie de investigaciones (39 casos) no se obtuvieron resultados positivos ni con los tests de aglutinacion directa ni con la técnica de Coombs.

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(Chief: Professor Curt Gyllenswärd.)

Elephantiasis Congenita Angiomatosa

by HERBERT ENELL and BIRGER HAHN

The paediatrician and the child surgeon are not infrequently confronted by a form of congenital malformation of the angiomatous type, which is characterized by a diffuse, ill-defined, increase in the tissues and often involves an entire part of the body. The changes are usually confined to an arm or a leg, but may occur at multiple sites. The anatomical basis is a mixed haemo-lymphangioma with a preponderance in one or the other direction.

The literature, including the large text-books of paediatrics, provides very varying and often incomplete descriptions of this pathological condition. Moreover, there are considerable discrepancies in the data regarding its pathogenesis and prognosis. Because we have had a number of cases at our hospital, we have been obliged to form a definite opinion with regard to these questions, as well as to various forms of therapy. An account of our experience is given in the following.

NONNE in 1891 published a report of a family in which elephantiasis of the legs occurred as a congenital-hereditary phenomenon. In the following year, MILROY described a family in which 20 out of 97 persons suffered from congenital oedema of the legs and in an additional two it developed at a later age. A few years later, MEIGE reported a further 8 cases. On the basis of these publications, and mainly in view of the symptomatology, it has become customary to regard Nonne-Milroy-Meige's disease or chronic hereditary oedema as a separate clinical entity. It is stated to be a hereditary-familial disease and to be consistently localized to the lower extremities (BRAHAM & HOWELLS; MEIGE; MILROY; SCHROEDER & HELWEG-LARSEN). The data regarding the onset of the disease nevertheless vary; thus all MEIGE's cases started during puberty. All the writers agree that, in this disease, the functional ability of the affected extremities is well maintained and that the condition is, on the whole, stationary. With regard to the pathogenesis, opinions are divergent and often based on hypotheses; conclusive histological studies are lacking. The most complete investigation appears to have been made by SCHROEDER & HELWEG-LARSEN, who described 11 cases; biopsy was performed in 4 of them. Fibrosis of the subcutaneous tissues then appeared to be the most salient feature, whereas the changes in the blood vessels and lymphatics were considerably less prominent.

The isolated cases of non-familial congenital elephantiasis — ELTERICH & YOUNT and ALLEN *et al.* — differ from the aforementioned description. The clinical picture is fairly similar to that in Milroy's disease, but the histological basis of the malforma-

tion, which is localized to one or several extremities, consists of an increased number of dilated blood vessels, particularly in the subcutaneous tissue.

In their monograph on peripheral vascular diseases, EDGAR ALLEN *et al.* presented a classification of 300 cases of different forms of lymphoedema as follows:

I. Non-inflammatory
  A. Primary
    1. Lymphoedema praecox
    2. Congenital lymphoedema
      a. Hereditary or familial (Milroy's disease)
      b. Simple
  B. Secondary
    1. Malignant occlusion
    2. Surgical removal of lymph nodes
    3. Pressure
    4. Roentgen and radium therapy

II. Inflammatory

They emphasized that the term "Milroy's disease" should be reserved for lymphoedema which is both congenital and hereditary. They described 12 cases which they designated as simple congenital lymphoedema, and none of the familial form. Theirs is the most complete description of the pathological findings that we have been able to find in the literature. The authors concluded by suggesting the term "congenital lymphangiectasis" to replace the term "congenital lymphoedema". POTTER interpreted this type of malformation as oedema based on angiomatosis. All the cases described in the following conform closely to this non-familial congenital elephantiasis, which we have preferred to designate as *elephantiasis congenita angiomatosa*.

During the neonatal period, so-called lymphangiectatic oedema is fairly often present, particularly on the dorsal aspects of the hands and feet, but in a considerably milder form than in the aforementioned disease. It consists of accumulation of fluid in abnormally wide lymphatic spaces in the skin, and subsides rapidly. It disappears entirely two months after birth. From the point of view of a differential diagnosis, there are also a number of forms of elephantiasis which occur secondarily to lymphostasis of various origin, such as through scar-formation, lymph node processes and intraabdominal tumours.

Elephantiasis congenita angiomatosa usually causes changes which are noticeable at birth, in the form of diffuse thickening of the soft tissues. The skin often has a normal appearance but palpation shows the subcutaneous tissues to be thickened. As a rule, there is no pitting, as in oedema produced by fluid. During the period of growth there is often progression, but a stationary condition may be reached before the end of this period. In some cases the changes are so slight at birth that they are not noticed until later in childhood. In addition to hypertrophy of the soft tissues, some elongation of the

bones in the affected part of the body may take place gradually, secondary to the vascular malformation. Impaired function of the affected extremity is only found in such cases in which the increase in the soft tissues is so pronounced that it results in mechanical limitation of the movements of the joint. Thus, the functional ability of the affected extremity is surprisingly intact, and the general development is, as a rule, normal.

A definite diagnosis can only be made by means of biopsy and histological examination of the specimen. The microscopical picture is then that of an angioma of varying degrees of differentiation. It ranges between an entirely typical haemangioma and lymphangioma, and vascular spaces, covered by endothelium, of undifferentiated type and fairly irregular arrangement. The margins of the vascular changes are poorly defined. The lesions are usually confined to the subcutaneous tissues, but may also involve the muscles, and at times the blood vessels, nerves and bone tissue. A markedly infiltrative growth is not infrequently seen, and the more primitive types of angioma may become malignant and be transformed into an angiosarcoma.

During the past 10 years, altogether eight cases of elephantiasis congenita angiomatosa have been treated at the medical and surgical clinics of Kronprinsessan Lovisa's Hospital for Children.

Case-reports

CASE 1. F. A girl, b. March 18, 1951. Birth weight 3450 g. One sib was alive and healthy. A maternal uncle had a congenital branchial cyst; nothing else of interest was found in the hereditary history. The mother's pregnancy and parturition were normal. At birth (Fig. 1) the whole left leg, the left gluteal region and the flank, up to the level of the umbilicus, were considerably swollen. There was a dark, bluish-red discoloration of the skin, which was tense and felt colder on the left than on the right leg. A slight, ulcerous patch of gangrene was present on the flexor aspect of the ankle. The circumference of the left thigh was 28 cm. and that of the right 13; the corresponding figures for the calf were 24 and 10 cm., respectively. There were no pathological symptoms from the internal organs or other discernible malformations. X-ray examination showed a considerable increase in the soft-tissue shadow from the foot and upwards in the left flank, but no skeletal changes. The image of the soft tissues corresponded approximately to that in marked "chronic oedema".

On admission there was anaemia and a tendency to haemorrhage in the form of numerous petechiae over the whole body. The patient subsequently became increasingly lethargic and icteric and her general condition deteriorated, with signs of septicaemia. Death occurred on the third day.

Autopsy showed the direct cause of death to be bilateral subdural haematomata and subarachnoidal haemorrhages. The left femoral vein was constricted by a number of pea- to bean-sized nodules. The muscles of the left leg were considerably infiltrated with blood but no clots were visible.

Histological diagnosis: an infiltrative angioma was present in the muscles; it consisted mainly of wide, blood-filled capillaries, of cavernuos appearance in some areas (Fig. 2).

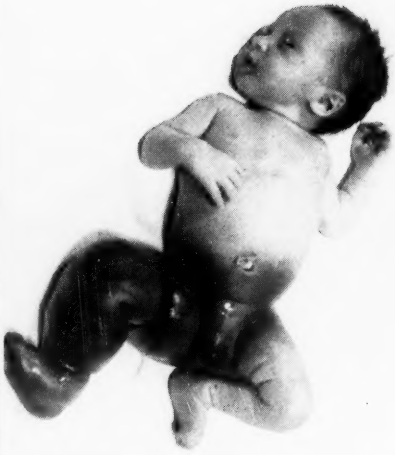

Fig. 1. Undifferentiated infiltrative angioma. (Case 1.)

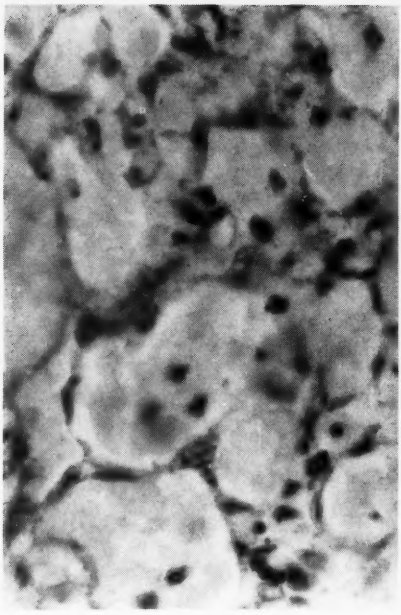

Fig. 2. Microscopical view of muscle: capillaries of cavernous appearance and solid areas with undifferentiated cells. (Case 1.)

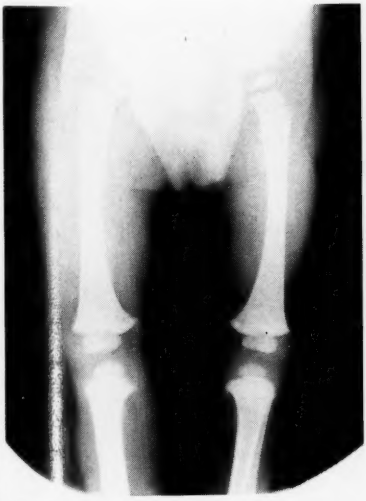

Fig. 3. Soft-tissue radiography: spongy image of the subcutaneous tissues of the right thigh. (Case 2.)

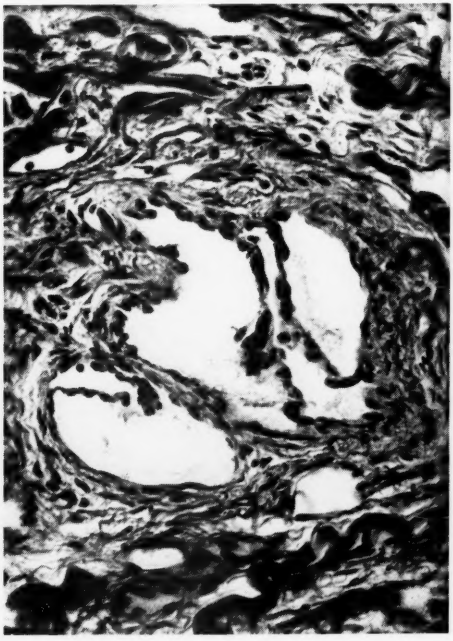

Fig. 4. Subcutis of the right leg: lymphangioma. (Case 2.)

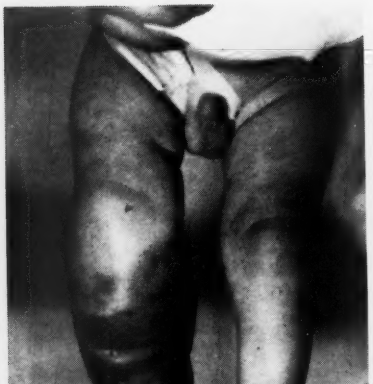

Fig. 5. Lobulated haemangioma of the cutis. (Case 3.)

Fig. 6. Granular and spongy structure of the soft tissue. (Case 3.)

Fig. 7. Elephantiasis congenita; after operation malignant growth (angiosarcoma) with metastases. (Case 6.)

In addition, there were more solid areas, rich in cells, with small capillary vessels. The lymph nodes exhibited fibrosis (S. Sjöberg).

CASE 2. O.J. A boy, b. April 7, 1950. Birth weight 2420 g. Nothing of interest was found in the hereditary history. The mother's pregnancy was normal. The patient was a dizygotic twin. His twin sister died on the second day of life of asphyxia, she had no malformations; there were no other sibs. The right leg was thicker and firmer than the left at birth; there was subsequently an increase in the hypertrophy.

The patient was admitted to our hospital at the age of eight months. The circumference of the right thigh was then 3 cm. more than that of the left. The skin was normal, but palpation showed the subcutaneous tissue to be thicker in the right leg. There was no pitting and no limitation of movement. X-rays of the skeleton revealed no pathological changes and no definite difference in the length of the legs. Soft-tissue radiography showed a strange, spongy image of the subcutaneous tissues (Fig. 3), particularly in the panniculus adiposus, indicating a considerable accumulation of fluid in the connective tissue spaces of the subcutis. Oscillography showed no definite difference between the legs. *Biopsy:* No pathological changes in the skin or muscles. Subcutis: multiple, small, dilated lymph vessels were present particularly in the connective tissue (Fig. 4) with damage to the endothelium and rounded, more prominent nuclei than normally; scattered proliferation of the endothelial cells (H. Bergstrand).

The patient was kept under observation for more than a year. At the end of that time the hypertrophy was stationary, but the right leg was 2 cm. longer than the left. The functional ability was slightly impaired, but the general development was normal. No therapy was attempted. At the age of two, the patient was operated on for hydrocele on the right side.

CASE 3. B.S. A boy, b. Dec. 12, 1944. Birth weight 3720 g. No. 2 of two sibs. Nothing of note was found in the hereditary history. The mother's pregnancy was normal. Since birth there was an increasing, bluish discoloration and enlargement of the left leg. At the age of four months, the circumference of the right calf was 24 cm. and that of the left 10 cm. (Fig. 5). The leg was firm and elastic, like fairly hard rubber in consistency; it was bluish-red in colour with sharply defined margins below the knee and in the centre of the instep. There was no objective tenderness. A firm nodule, the size of a walnut, was palpable in the left groin. X-rays of the leg (Fig. 6) showed no skeletal changes, but a strange soft-tissue structure, with a "granular" image and sharp margins, indicating vascular malformation. *Biopsy:* a lobulated haemangioma, consisting of thin-walled vessels and clusters of angioblasts, was present in the deeper layers of the cutis and in the lymph nodes (H. Bergstrand).

X-ray treatment was given and the patient was kept under the observation of an orthopaedic surgeon; support was applied to the leg as a palliative measure. The changes progressed and walking became difficult. At the age of six the circumference of the right calf was 29 cm. and that of the left 22 cm. The skin was eczematous and slightly damp. The swelling was fairly firm in consistency. Arteriography on Dec. 11, 1950 through a percutaneous puncture in the right femoral artery showed extensive vascular malformations in the whole leg below the knee, particularly around the ankle; they were most pronounced in the region of the anterior tibial artery. Operation was performed on the same day: the anterior tibial artery was ligated and ethanolamine oleinate (Etolein, Astra) injected. Post-operative arteriography showed improvement in the circulatory conditions. During the year prior to writing there has been definite subjective and objective improvement; the patient is now able to ski.

CASE 4. B.H. A girl, b. June 4, 1949. Birth weight 4000 g. Two whole sibs and two half sibs healthy. Nothing of note was found in the hereditary history. Since birth there was considerable swelling of the whole left leg, involving four diffusely-defined areas with a more marked increase in consistency. Extirpation was performed in two stages, at 2 and 10 months, respectively, at a hospital in Finland. *Biopsy:* lymphangioma (E. Saxén). As there was still progression of the lesions, new incisions were made at our hospital when the patient was 18 months old. *Biopsy:* lymphangiolipoma with no signs of malignancy (H. Bergstrand). The malformation then caused little inconvenience; the child could walk without difficulty. No other malformations were found. As the angiomatosis recurred, a course of subcutaneous injections of ethanolamine oleinate was given at the age of two; up to the time of writing the results have been satisfactory, although there is slight limitation of movement.

CASE 5. I.F. A girl, b. Dec. 12, 1949. Birth weight 3500 g. Nothing of note was found in the hereditary history; there were no sibs. At birth, the left hand and forearm were found to be considerably swollen. The swelling increased successively and the patient was admitted to our hospital at the age of 8 months. The whole left arm was then hypertrophic with a diffuse swelling of the soft tissues, most pronounced on the dorsal aspect of the hand. The circumference of the left forearm was 20 cm. and that of the right 12.5 cm.; the circumference of the left hand was 22.5 cm. and that of the right 10 cm. The functional ability was surprisingly good. The right side of the face and the ear were also slightly swollen. X-rays showed a coarse-meshed image of the soft tissues of the left arm, with the same "granular" appearance as in Case 3. The patient was transferred to the plastic surgery unit of Serafimerlasarettet. The skin and subcutaneous tissues were excised in several stages. *Biopsy:* lymphangioma with no signs of malignancy (B. Falconer). In the middle of June 1951, the patient became ill: the stools were frequent and watery, the systemic disturbances became increasingly severe, with ascites and oedema of the legs. The condition of the left arm remained unchanged. The patient died after six weeks' illness.

Autopsy revealed lymphangiomata, with endothelial proliferations not only in the forearm but also in the small intestine and the mesentery. The tumour formations were poorly defined but showed no signs of malignancy (S. Olsson).

CASE 6. B.L. A girl, b. March 24, 1939. Birth weight 3700 g. No. 3 of three sibs; the older sibs were healthy. No hereditary history of malformations. The mother's pregnancy was normal. There was congenital hypertrophy of the whole right arm, which remained fairly stationary until the patient was admitted to our hospital at the age of two years (Fig. 7). The functional ability was then good and the general development normal. The right arm evidenced diffuse swelling; the circumference of the forearm was 19.5 cm. and that of the left forearm 13.5 cm. The corresponding figures for the hand were 16.5 and 12 cm., respectively. The right arm was 1 cm. longer than the left. X-ray examination showed no skeletal changes, but considerable swelling of the soft tissues and a strange, spongy image. A plastic operation was performed according to Condoleon's technique in the surgical department. Nothing definitely pathological was found on histological examination (H. Bergstrand). Post-operatively, an ulcer developed in the scar on the forearm. Several years later this ulceration became transformed into a tumour, somewhat larger than a walnut. It was removed by curetting in 1946. *Histological examination* showed a haematoma and inflammatory lesions. Despite increasing hypertrophy, the arm functioned satisfactorily. It was necessary to make two further curettages; histological examination on Nov. 11, 1947 showed

a malignant growth of the angiosarcoma type. Pulmonary densities were found at the same time; they were presumably metastases. After slow, successive exacerbation, the patient died at home in June, 1949. No autopsy was performed.

CASE 7. I.J. A girl, b. June 26, 1946. Birth weight 3250 g. No. 2 of two sibs. Nothing of note was found in the hereditary history. From birth there was considerable swelling of the right foot and moderate swelling of the left foot and fingers. The functional ability was unimpaired and the general development normal. The patient was admitted to our hospital at the age of three years. There was then appreciable, cushioned swelling of the dorsal aspect of the right foot and less marked swelling over the left instep and the fingers of both hands. Arteriography showed no particular pathological changes. No skeletal changes were found on X-ray examination; X-rays of the soft tissues of the foot showed a coarse-meshed image. *Biopsy:* neoplastic strands of connective tissue with numerous, fairly fine-calibered lymphatic vessels were present in the cutis and, to a still greater extent, in the subcutaneous adipose tissue. The collagen fibres in the cutis were thickened. Lymphangiomatous skin malformation (H. Bergstrand). No therapy was applied.

Three years later there was still some swelling of the right foot, but possibly less marked; no functional limitation.

CASE 8. K.S. A boy, b. July 27, 1946. Birth weight 4200 g. No. 3 of three sibs. Nothing of interest was found in the hereditary history. Multiple congenital malformations were present: there was a soft, cystic tumour, the size of an orange, on the left side of the throat and similar, smaller tumours on the right side of the neck and in the right axilla. Both hands were considerably deformed, with some fingers missing. The soft tissues of the right hand and forearm were greatly swollen. X-ray examination at the age of 2 months also revealed an expansive process in the upper part of the mediastinum. This was diagnosed as a probable lymphangioma, and X-ray therapy applied to it and to the cervical tumours. The latter subsequently diminished but after a further six months began once more to grow. The mediastinal process was unaffected by therapy and instead showed slow progression. Repeated courses of sclerosing therapy were given to the right arm and the neck but had no demonstrable effect. X-ray examination of the soft tissues showed a "lumpy" image, which seemed to indicate an irregular dilatation of the small blood vessels rather than oedema. The patient's general condition remained relatively unaffected; his general development was normal and the functional ability fairly good.

At the age of four, the patient had a haemorrhage from the mediastinal tumour, resulting in compression of the trachea; he died within three hours. The clinical diagnosis was multiple lymphangiomatosis. *Autopsy* showed a cavernoma of the lymphangiomatous type in the mediastinum, without malignant infiltration (I. Behring).

Discussion

The malformations were congenital in every case. No hereditary factors or sex preponderance could be found. One leg was affected in four cases and one arm in three. In one case the angioma was present in one hand and one foot; there was concurrent lymphangiectatic oedema, a combination which is stated to be not uncommon. In the majority of cases the lesions were severe. The diagnosis of elephantiasis congenita angiomatosa was estab-

TABLE

Case	Sex	Pres. Age Yrs.	Localization				Microsc. Diagn.			Course		Theraphy			Present Condition		
			Hand	Arm	Foot	Leg	Lymph-angioma	Haem-angioma	Undiff.	Re-gress	Pro-gress	X-ray	Oper.	Scle-ros.	Impr.	Unch.	Dead at
1. F.	♀	—				+			+		+						3 dys.
2. O. J.	♂	2				+	+				+					+	
3. B. S.	♂	7				+		+			+	+		+	+		
4. B. H.	♀	$2^1/_2$				+	+				+		+	+	+		
5. I. F.	♀	—		+			+				+		+				$1^1/_2$ yrs.
6. B. L.	♀	—		+			+	→	+		+		+				10 yrs.
7. I. J.	♀	$5^1/_2$	+		+		+			+		(+)			+		
8. K. S.	♂	—		+			+				+	(+)		+			4 yrs.

lished by biopsy, except in two cases in which the diagnosis was made at autopsy. In six cases histological examination revealed lymphangiomatous tissue, in one a typical diffuse haemangioma and in one a more undifferentiated angioma. In Case 6, in which repeated biopsies were performed in connexion with plastic operations, the picture gradually developed into that of an angiosarcoma.

In 7 out of the 8 cases *X-ray examination of the soft tissues* was made. Later study of the films showed that the structure of these tissues exhibited typical changes of the nature described earlier in the case-reports. An example is furnished by the X-ray pictures of the extremities in Case 3 (Fig. 6), in which the strikingly spongy and loose structure of the subcutaneous tissue is apparent. Thus, in such malformations, soft-tissue X-rays (according to FRANTZELL) provide certain diagnostic possibilities. In many cases they point directly to an angiomatous type of tissue lesion, whereas in some of the cases described they only showed diffuse oedema.

With regard to the *course*, it was found that the untreated malformations showed a distinct tendency to progression. Only in one case in which there was concurrent lymphangiectatic oedema was spontaneous regression noted: definite swelling of one foot nevertheless persisted when the patient was $5\,^1/_2$ years old.

Various forms of *therapy* have been attempted. Irradiation of lymphangiomatous tissue is considered to be valueless. In one case, however, in which a haemangioma was present, it was given in the form of X-ray therapy but was ineffective. In three cases various forms of plastic operations were performed. In one case this resulted in temporary improvement, but subsequent progression caused so-called sclerosing therapy to be substituted. In the two other cases treated surgically by removal of the angiomatous tissue, a local recurrence took place fairly soon after operation. In Case 6, the angioma degenerated into an angiosarcoma with metastases to the lungs.

In three cases, so-called sclerosing therapy — *i. e.*, injection of ethanolamine oleinate into the angioma — was tried. Subcutaneous injections led to improvement in the patient who had been operated on earlier. In one case the anterior tibial artery was ligated, and ethanolamine oleinate injected; the results were also satisfactory. In the third case, subcutaneous injections of ethanolamine oleinate were given concurrently with X-ray treatment of the angioma on the neck and in the mediastinum. No opportunity was afforded of observing the final results, since the patient died suddenly.

No other methods of treating this disease than those already mentioned are described in the literature. In our experience, therapy only results in temporary improvement and the tendency to recurrence is great. The risk of malignancy after a surgical intervention must also be envisaged.

Summary

An account is given of eight cases of congenital elephantiasis with angiomatosis, in which no hereditary history of the disease was found. It is emphasized that a definite diagnosis can be made by means of histological examination, and that soft-tissue radiography may often facilitate the diagnosis. The prognosis with regard to spontaneous regression is found to be poor, but the functional ability is usually relatively unimpaired. Various forms of therapy are discussed. In one of the four deaths, the cause was found to be malignancy of the growth.

Angiomatose congénitale avec éléphantiasis.

Les auteurs présentent 8 cas de l'éléphantiasis congénital avec angiomatose, chez lesquels on ne retrouve pas de caractère héréditaire. Ils posent que le diagnostic définitif peut être assuré grâce à l'examen histologique et que la radiographie des parties molles peut faciliter celui-ci. La régression spontanée est rare, mais le pouvoir fonctionnel reste relativement normal. Diverses thérapeutiques sont discutées. Dans un des 4 cas morts, la cause de la mort était l'évolution maligne de la maladie.

Angeborene angiomatöse Elephantiasis.

Eine Übersicht über 8 Fälle von angeborener angiomatöser Elephantiasis, bei welchen keine Erbanamnese des Leidens gefunden wurde, wird vermittelt. Es wird hervorgehoben, dass die endgültige Diagnose durch die histologische Untersuchung gestellt werden kann, und dass die Weichteilradiographie die Diagnose erleichtern kann. Die Prognose ist in Bezug auf spontane Rückbildung schlecht, die funktionelle Tüchtigkeit ist gewöhnlich relativ unbeeinflusst. Verschiedene Therapieformen werden diskutiert. In einem der vier Todesfälle war die Bösartigkeit des Wachstums die Todesursache.

Elefantiasis congénita angiomatosa.

Se describen ocho casos de elefantiasis congénita con angiomatosis, en los que no se encontró ninguna herencia de la enfermedad. Se subraya que puede hacerse el diagnóstico definitivo por medio del examen histológico y que la radiografía del tejido blando facilita amenudo el diagnóstico. Se encuentra que el pronóstico con respecto a una regresión espontánea es demasiado inseguro, pero la habilidad funcional está en general relativamente inalterada. Se discuten varias formas de terapéutica. En uno de los cuatro casos fallecidos se encontró que la causa era una malignidad del desarrollo.

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Comparative Studies on the Bone-marrow, Blood and Gastric Juice Culture of Tubercle Bacilli in Children

by C. CHOREMIS and C. DANELATOU

In a preliminary communication on the presence of the tubercle bacillus in bone-marrow (CHOREMIS, PANTAZIS) we have reported that the percentage of positive bone-marrow cultures has been found to be high (24.5 %) even in cases of primary complex. *In the technique used bone-marrow was inoculated in amounts of 0.1—0.2 cc directly into Löwenstein and Petragnani media.*

Since the communication of this paper, 85 more cases have been examined. Beside bone-marrow cultures, blood cultures and gastric juice cultures were simultaneously performed. The above cases were all children between 3 months and 13 years, suffering from different forms of tuberculosis, i.e. primary infections (51 cases), t.b. of serous membranes (9 cases), miliary tuberculosis (9 cases) and t.b. meningitis (16 cases).

Results

a. Primary complex. Bone-marrow, blood and gastric juice cultures were taken from 51 cases of primary complex. In the 17 of them at least *one* culture became positive; 19 positive cultures were obtained. Of them 11 were bone-marrow cultures, 5 gastric juice cultures and only 3 blood cultures.

b. T.b. of serous membranes. Cultures were taken from 9 cases. There were 3 positive bone-marrow cultures.

c. Miliary tuberculosis. Six out of the 9 cultures of miliary tuberculosis became positive. Four were bone-marrow cultures and 2 gastric juice cultures. All the blood cultures were negative.

d. T.b. meningitis. Nine of the 16 cases studied gave at least one positive culture. Twelve positive cultures were obtained. Of them 8 were bone-marrow cultures, 2 gastric juice cultures and 2 blood cultures.

As can be seen from the analysis of the results obtained, in all groups bone-marrow cultures proved to be more successful than gastric juice or blood cultures.

We would like to emphasize that all cultures were systematically *subcultured even in those that appeared to be negative.*

We believe this to be advisable, since many of the negative or suspicious cultures became positive when subcultured. Direct smear for acid fast bacilli were positive in most of the negative cases which became positive when subcultured. We think therefore that a culture for t.b. should not be considered negative unless the subculture proves to be negative also. The subcultures have been biologically controlled by animal inoculation in Prof. Melanides' Laboratory (High Agricultural School).

Discussion

The subject of bone-marrow cultures in t.b. has been studied in the past, especially in adult patients. Positive bone-marrow cultures were first obtained from material taken post-mortem (KIOZUMI, LÖWENSTEIN, BEZANÇON, BIERNACKI). Later E. BERNARD, EVEN, S. KATZ, cultured bone-marrow from adult patients. They prepared the material in a way similar to the one used for blood or sputum and obtained positive results in a relatively high frequency (KATZ 89 % positive results in acute haematogenous tuberculosis, E. BERNARD 18 % positive results in miliary tuberculosis). DÉBRÉ *et al.* were the first to study bone-marrow cultures in children. Their cases suffered from a progressive form of t.b. Despite the positive results obtained and the great interest this problem presents, the authors did not arrive at any definite conclusions, their observations on this subject being very limited.

We believe that the relatively frequent occurrence of t.b. bacillus in bone-marrow could be explained on the following grounds:

a. The blood supply of the bone-marrow is rich especially in children.
b. The blood circulation is relatively slow.
c. The bone-marrow as part of the reticuloendothelial system has a selective ability (affinity) to retain microorganisms.

The superiority of bone-marrow cultures against blood cultures is not encountered in tuberculosis alone, but in other infectious diseases as well. Therefore the bone-marrow cultures are systematically used in our clinic. As already known (MILTON-SACKS, HIRSOWITZ, CHOREMIS—LAZARIDES) bone-marrow cultures in typhoid fever are found positive in a greater frequency than blood cultures. Work done in our Clinic has shown that in purulent meningitis bone-marrow cultures are found positive almost as frequently as C.S.F. cultures, 30 % and 31 % respectively (CHOREMIS—ATHANASSIADES) and much more frequently than blood cultures. We believe that the finding of t.b. bacillus in bone-marrow has a theoretical as well as a practical im-

portance. Of particular interest for the evolution of t.b. in children is the relatively high frequency of positive bone-marrow cultures as well as the finding of t.b. bacillus in the blood and the C.S.F (CHOREMIS—VRACHNOS, CHOREMIS *et al.*) in cases of primary complex without clinical manifestations. The above findings compell us to change our ideas about the meaning of the primary complex and its relation to the whole pathogenesis of t.b. We have been used to consider the primary complex rather in a static sense. It is apparently a dynamic process which much more often than we think results in a dissemination and localisation of t.b. bacilli in other tissues and especially in the reticuloendothelial system. We think therefore that the primary complex and its relation to the evolution of tuberculosis should be reconsidered in a wider sense.

Summary

Bone-marrow (bm), blood (b) and gastric juice (gj) cultures have been taken from 51 cases of primary complex (bm. 11, b. 3, gj. 5 pos.), 9 cases of t.b. of serous membranes (bm. 3, b. 0, gj. 0 pos.), 9 cases of miliary tuberculosis (bm. 4, b. 0, gj. 2 pos.) and 16 cases of t.b. meningitis (bm. 8, b. 2, gj. 2 pos.). The practical and theoretical importance of these findings is discussed.

Etudes comparatives sur la culture de bacille de Koch de la moëlle osseuse, du sang et du suc gastrique.

Les auteurs firent des cultures de bacille de Koch de la moëlle osseuse (Mo), du sang (S) et du suc gastrique (Sg) issus de 51 cas de primo-infection (Mo 11, S 3, Sg 5 pos.), 9 cas d'atteinte des séreuses (Mo 3, S 0, Sg 0 pos.), 9 cas de granulies (Mo 4, S 0, Sg 2 pos.) et 16 cas de méningite tub. (Mo 8, S 2, Sg 2 pos.). Discussion pratique et théorique de ces travaux.

Vergleichende Studien über Knochenmark-, Blut- und Magensaftkulturen von Tuberkelbazillen bei Kindern.

Knochenmark- (Km), Blut- (B) und Magensaftkulturen (Ms) wurden von 51 Fällen von tuberkulösem Primärkomplex (Km 11, B 3, Ms 5 pos.), 9 Fällen von Tuberkulose der serösen Häute (Km 3, B 0, Ms 0 pos.), 9 Fällen von Miliartuberkulose (Km 4, B 0, Ms 2 pos.) und 16 Fällen tuberkulöser Meningitis (Km 8, B 2, Ms 2 pos.) entnommen. Die praktische und theoretische Bedeutung dieser Befunde wird diskutiert.

Estudios comparativos de cultivos de bacilos tuberculosos de la médula ósea, sangre y jugo gástrico en niños.

Se hicieron cultivos de la médula ósea (mo), sangre (s) y jugo gástrico (jg) de 51 casos de complejo primario (mo 11, s 3, jg 5 pos.), 9 casos de tuberculosis de las membranas serosas (mo 3, s 0, jg 0 pos.), 9 casos de tuberculosis miliar (mo 4, s 0, jg 2 pos.) y 16 casos de meningitis tuberculosa (mo 8, s 2, jg 2 pos.). Se discute la importancia práctica y teorética de estos encuentros.

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Electroencephalographic Studies of Asthmatic Children

by BÖRJE HOLMGREN and SVEN KRAEPELIEN

It has long been known that bronchial asthma concerns not only the lungs and the circulation system. The effect of this disease on the central nervous system, with particular regard to the occurrence of a cerebral allergy, has long formed the subject of debate. The introduction of electroencephalographic investigation methods (EEG) facilitated a closer study of these questions.

Dess and Lowenbach, in 1948, published an investigation in which these conditions had been studied by means of EEG in a group of allergic children. Their series comprised 85 children, aged 2—14 years, suffering from various allergic diseases (56 cases of asthma). They found that, according to their criteria, pathological EEG occurred in 3/4 of their cases (i.e. in 65 out of 85). However, it should be noted that their series included 22 children with convulsive diseases (petit mal and grand mal) combined with different allergic manifestations. Also, the prerequisites for a pathological EEG were considerable, to judge from present experience of EEG on children in general. They noticed a definite correlation between the duration of the disease and the EEG changes, as well as between positive allergic heredity and pathological EEG. The dominating EEG change was a slow occipital dysrhythmia, ascertainable in half of the examined cases. In a similar inquiry, comprising 80 allergic children without any signs of convulsive diseases, Chobot, Dundy and Pacella (1950) found pathological EEG in but 1/3 of their patients. The asthmatic children numbered 52 and EEG changes were detected in 16. Also these investigators established a correlation between the duration of the disease and the frequency of the pathological EEG.

The above-mentioned investigation results struck the present authors as noteworthy. Therefore, during the past few years, a study of those conditions was made as a matter of routine, on a comparatively large group of asthmatic children, taken from the Pediatric Clinic of Karolinska Sjukhuset in Stockholm (Kraepelien). The aim was to obtain series which was as unmixed as possible.

The case series

One hundred asthmatic children, aged 2—15 years, were examined, with a sex distribution conforming to that generally noticed in groups of asthmatic children (viz. 37 girls and 63 boys). The age distribution is illustrated in Fig. 1, 4/5 of the series representing children 4—9 years of age.

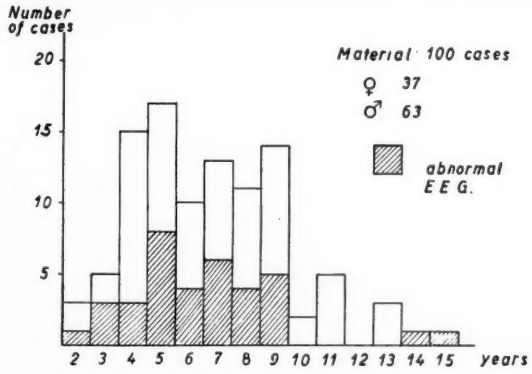

Fig. 1. Age distribution and the occurrence of pathological EEG in the various age-groups.

The children were chosen at random for the investigation. Nervertheless, a certain selection is to be noted in so far as children with a hereditary predisposition for convulsive diseases, or showing signs of a convulsive disease, or with a known birth injury, or known cerebral injury sustained later, were excluded from the investigation. The duration of the children's asthma disclosed considerable variations, from 1—12 years, averaging 4—5 years. The degree of severity of their asthma also varied markedly. The cases were, consequently, classified in three groups, as follows: a mild, a medium severe and a severe asthma group. The mild asthma group includes only cases with 4—5 real attacks yearly (27 cases), the medium severe group cases with 6—12 attacks yearly (46 cases), and the severe group iterated attacks with long periods of status asthmaticus (27 cases). About 3/4 of the series, therefore, consists of a moderately severe or severe asthma. Apart from asthma, some of the children manifested also other allergic symptoms, such as urticaria, eczema and allergic cold.

Method

The electroencephalographic examinations were carried out with a 6-channel, direct-recording, Grass apparatus, with uni- as well as bipolar recording from 12 electrodes (6 on each hemispere) for 15 minutes, with a hyperventilation test for 3 minutes (Holmgren). All the examinations took place when the children were free from symptoms without any symptomatic treatment, or had only isolated rhonchi on auscultation of the lungs.

Results

EEG changes of different degrees of severity were recorded in 36 of the examined cases (i.e. 36 %). The frequency of pathological EEG in the different age-groups is set down in Fig. 1.

The nature of the EEG changes varied (see Table 1), 15 cases showing a marked dysrhythmia and the remaining 21 moderate but definite dys-

TABLE 1

Nature of EEG changes in the 36 pathological cases.

	Number of cases
Degree of dysrhythmia	
Strong	15
Moderate	21
Type of dysrhythmia	
Slow dysrhythmia, most evident occipitally	22
Focal spikes or sharp-waves	3
General wave-and-spike episodes	3
Pathologically slow basic rhythm (α-activity)	9

rhythmic changes. However, no EEG changes significant of asthma were ascertained, though barely 2/3 of the pathological cases disclosed a slow occipital dysrhythmia.

The EEG changes in two asthmatic children of different age (4 and 8 years) are demonstrated in Figs. 2 and 3. For comparison with these pathological curves, a normal curve was included from each of the two age-groups.

No sex difference was noted in regard to the frequency of pathological EEG. Nor was any correlation found between the duration of the asthma and the frequency of the pathological EEG. The age of onset of the asthma did not seem in any way related to the frequency of the EEG changes. The children with a positive allergic heredity revealed the same percentage of pathological EEG as those without. On the other hand, in the present series the EEG changes seem to have a certain correlation to the degree of severity of the asthma. As may be seen from Fig. 4, half of the cases with severe asthma showed pathological EEG, while those with moderately severe or mild asthma had pathological EEG in a third or fourth of the cases.

All the children included in this series were examined during a free interval, i.e. when entirely or practically free from symptoms of asthma, and the observed EEG changes can therefore be regarded as comparatively permanent. For a further analysis of the effect of asthma on the EEG, children were examined also during an attack of asthma and immediately afterwards. Fig. 5 gives the observations on a 10-year-old girl who had suffered from severe asthma ever since the age of 1. The first recording was taken during a severe status asthmaticus, showing an EEG curve with clearly pathological conditions, while 8 days later, at a subsequent recording, the curve had been normalized after the asthmatic attack had subsided and the patient was almost entirely free from symptoms.

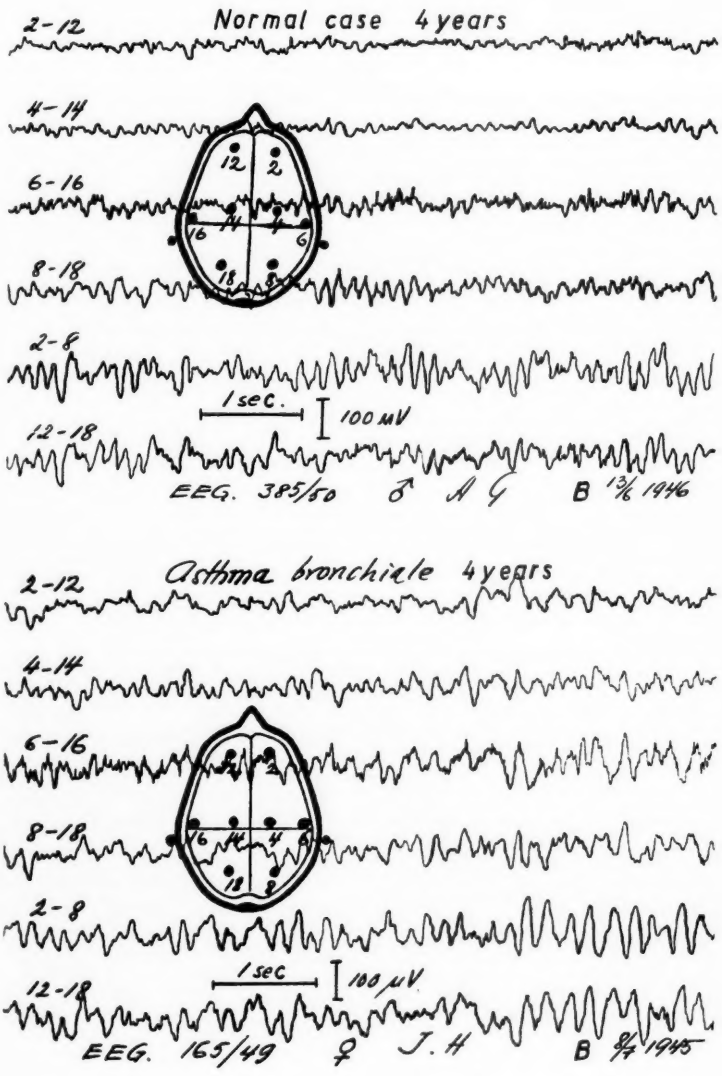

Fig. 2. EEG of a normal 4-year-old boy, compared with EEG of a girl of 4 with mild asthma since the age of 1.

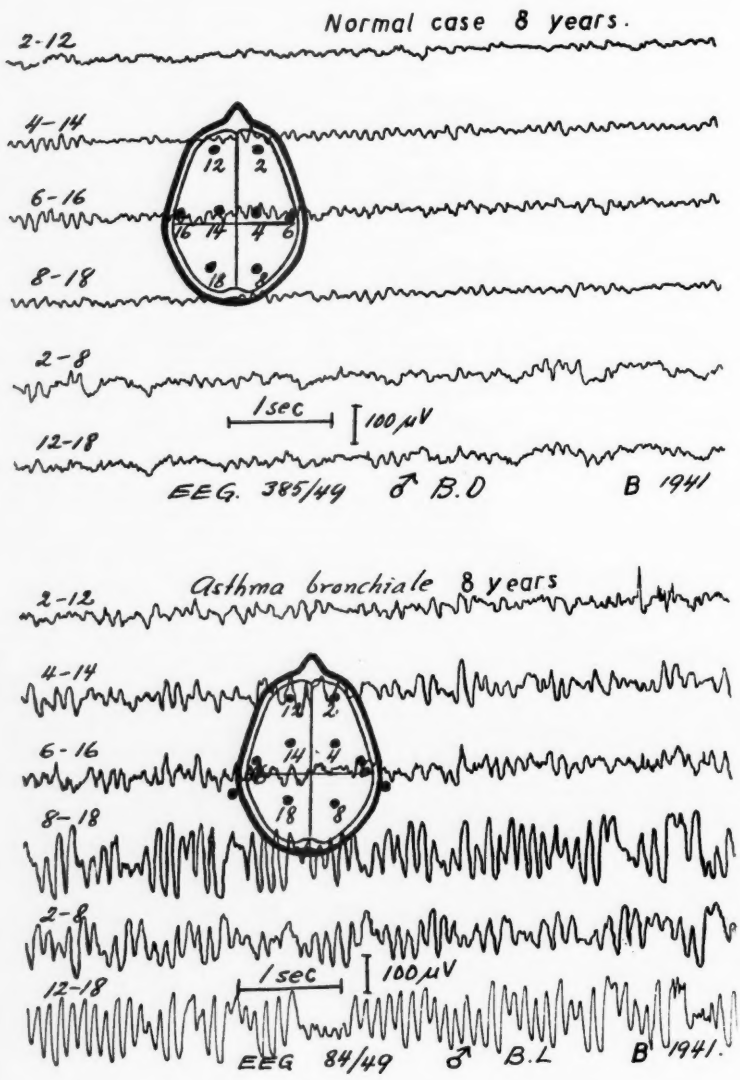

Fig. 3. EEG of a normal 8-year-old boy, compared with EEG of a boy of 8 with severe asthma since the age of 1.

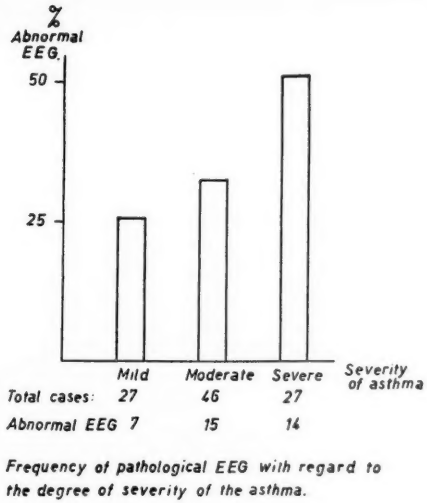

Fig. 4. Frequency of pathological EEG with regard to the degree of severety of the asthma.

Discussion

In conformity with CHOBOT and coworkers, in the present series pathological EEG were found in about 1/3 of the examined cases. However, we were unable to establish a correlation between the duration of the disease and the occurrence of EEG changes, as demonstrated by DESS and LOWENBACH, as well as by CHOBOT and coworkers. The present investigation indicates that pathological EEG occurs in greater frequency among cases with a more severe asthma than in mild cases. Unfortunately, however, the present series is too small to justify an establishment of this statistically. No EEG changes typical of asthma were observed, though like DESS and LOWENBACH and, later, DE TONI an occipital dysrhythmia was found to occur in the great majority of the pathological cases.

In a normal population of children comprising about 150 cases in the same age-groups as the children in the present investigation, only about 5 % dysrhythmic curves were noted. This figure is largely in agreement with results obtained by other investigators studying normal cases (LINDSLEY). Thus, the asthmatic children show a much greater frequency of EEG changes than a series of normal children. The question of why this is so naturally arises. No satisfactory answer can be given, however, and we are unfortunately forced to resort to mere speculation.

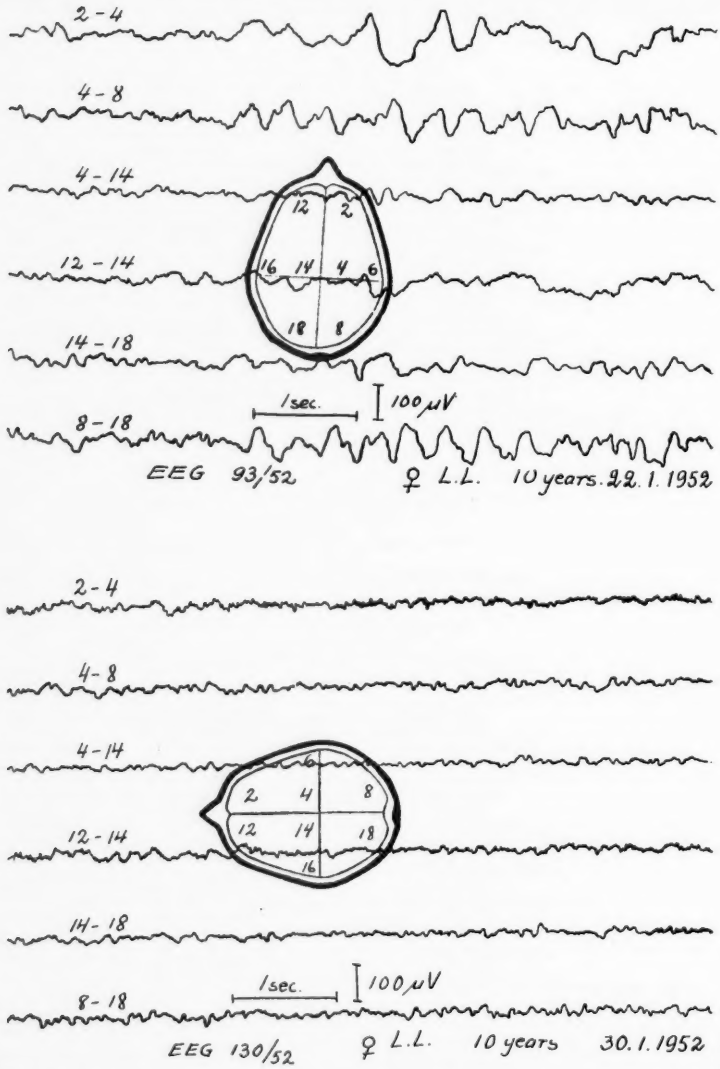

Fig. 5. EEG of girl of 10 during severe status asthmaticus and 8 days after.

22.1.52. Occipital basic rhythm (7/sec.) of fairly moderate occurrence. Comparatively abundant general occurence of medium-high 4/sec. waves and moderate 3/sec. waves with maximal amplitude occipitally, preponderating on right side. Slight occurence of low 9/sec. waves. Patient too weak to hyperventilate satisfactorily. Definitely pathological findings with signs of cerebral dysfunction, partly of focal type.

30.1.52. Occipital basic rhythm 7—9/sec. on an average, 8/sec. of sparse occurrence. Fairly moderate general occurrence of low 4—5/sec. waves. Slight beta activity. Hyperventilation moderately increases the slow dysrhythmia with regression within 1 min. Distinct regression, though not yet entirely normal finding.

It is conceivable that repeated asthmatic attacks may produce comparatively short or long states of hypoxia in the brain, with transient or permanent disturbances in the nerve cells of the brain. This derives support, inter alia, from the fact that the EEG changes are sometimes only temporary during the attack of asthma, disappearing after the attack.

Just as hypoxia in the brain of an asthmatic patient can be conceived as a direct consequence of failing pulmonary activity, the possibility cannot be ignored that the hypoxia may be due to the fact that in the brain of allergic subjects, as elsewhere in the body, generally typical allergic vascular changes may occur with vasoconstriction, perivascular infiltration and oedema, leading to a cerebral dysfunction. In neurodermatitis, a strikingly high frequency of pathological EEG (STERNBERG and BALDRIDGE) was observed, suggesting, inter alia, that in allergic subjects in general the allergic vascular changes in the brain cause the injures recorded in the EEG. The degree and nature of the vascular changes are decisive with regard to the temporary or more permanent occurrence of the EEG changes.

In 6 cases the EEG disclosed marked convulsion potentials with focal and general wave-and-spike episodes. This signifies that a latent convulsive disease is present without the patient having any clinical manifestations of convulsions. This is in conformity with observations made recently by DESS and LOWENBACH regarding the occurrence of purely allergic epilepsy.

Children with behaviour disorders disclose a high frequency of pathological EEG (JASPER). Though no particularly serious disorders of this kind have been discovered in the present series it should be borne in mind that these children, like series of asthmatic children in general, disclosed different degrees of neurolability. However, it was difficult in the present investigation to classify the children and study them more closely in this particular respect. The general lability of the children may be conceived to manifest itself in a dysfunction of the electrical activity of the brain with subsequent EEG changes.

Summary

1. One hundred children suffering from bronchial asthma, aged 2—15, without a hereditary predisposition for convulsive diseases, and without any convulsive manifestations of their own, were examined with regard to the occurrence of EEG changes.

2. Pathological EEG of different degrees and types occurred in 36 cases.

3. The type of EEG changes comprised partly a slow dysrhythmia — in about 2/3 of the cases most evident occipitally — partly focal spikes or sharp waves, in 3 cases, and general wave- and spike episodes in another 3 cases.

4. The occurrence of an allergic heredity, the duration of the asthma and the age of onset showed no correlation to the occurrence of EEG changes.

5. The degree of severity of the asthma seems to have a certain relation to the occurrence of pathological EEG.

6. During the acute attack of asthma, marked EEG changes were observed that subsided after the attack.

7. The facts underlying the EEG changes and their relation to the allergic condition are discussed.

Études éléctroencéphalographiques chez les enfants asthmatiques.

100 enfants atteints d'asthme bronchique, âgés de 2 à 15 ans, ont été examinés du point de vue EEG. Aucun ne présentait de prédisposition héréditaire ou personnelle en faveur de crises convulsives. Dans 36 cas le tracé était perturbé à des degrés différents. Les anomalies étaient les suivantes: légère dysrythmie (dans environ les 2/3 des cas les plus nets dans les régions occipitales), soit des pointes localisées ou des ondes pointues (3 cas) et enfin dans 3 autres cas des périodes de pointe-ondes généralisées. Aucune corrélation ne semble exister entre les modifications du tracé EEG et l'hérédité allergique, la durée de l'asthme et son début. L'intensité par contre des anomalies du tracé semblent être en rapport avec la gravité de l'asthme présenté. Pendant la crise aiguë les anomalies EEG importantes furent observées et elle subsidèrent après la crise clinique. L'auteur discute les rapports entre ces modifications de l'EEG et le facteur allergique.

Elektroencephalographische Untersuchungen bei asthmatischen Kindern.

Hundert an Bronchialasthma leidende Kinder im Alter von 2—15 Jahren ohne erbliche Vorbelastung für Krampfkrankheiten und ohne alle eigene Krampferscheinungen wurden in Hinblick auf EEG-Veränderungen untersucht. Ein pathologisches EEG von verschiedenem Grad und Typ wurde in 36 Fällen gefunden. Der Typ der EEG-Veränderungen beinhaltet teilweise eine langsame Dyrshythmie — in etwa 2/3 der Fälle am deutlichsten occipital — teilweise fokale Spitzen oder spitze Wellen, in 3 Fällen, and allgemeine Wave-Spike-Episoden in 3 anderen Fällen. Das Vorhandensein einer allergischen Anlage, die Dauer des Asthmas und das Alter des Auftretens zeigten keine Beziehung zum Vorliegen von EEG-Veränderungen. Der Schweregrad des Asthmas scheint zum Auftreten pathologischer EEG-Veränderungen in einem gewissen Verhältnis zu stehen. Während der akuten Asthmaattacken wurden deutlichere EEG-Veränderungen gesehen als nach den Attacken. Diskussion der Gegebenheiten, welche den EEG-Veränderungen zugrundeliegen und deren Beziehung zum allergischen Zustand.

Estudios encefalográficos en niños asmaticos.

Un centenar de niños, de 2—15 años de edad, que sufrian de asma bronquial sin predisposición hereditaria para enfermedades convulsivas y sin ninguna manifestación convulsiva por su propia parte, fueron examinados respecto a los cambios del EEG. EEG patológicos de diferentes grados y tipos aparecieron en 36 casos. Los tipos de los cambios del EEG contienen en parte una disritmia lenta — en aproximadamente 2/3 partes de los casos, lo mas evidente occipital — en parte puntas focales o intensas ondas, en 3 casos, y fases generales de puntas y ondas en otros 3 casos. La ocurrencia de una alergia hereditaria, la duración del asma y la edad de cada uno, no mostró ninguna correlación con los sucesos de los cambios del EEG. El grado de la severidad del asma parece tener cierta correlación con los sucesos de un EEG patológico. Durante el ataque agudo de asma, fueron observados cambios intensos del EEG que se apaciguaron despues del ataque. Se discuten los hechos subrayando los cambios del EEG y su relación con la condición alergica.

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CASE REPORTS

Familial Early Infantile Myasthenia Gravis

by B. BORNSTEIN, Tel Aviv (Israel)

The familial appearance of myasthenia is rare; cases, in which the disease appears in more than one member of the family are cited sporadically. These sporadic quotations are, however, important owing to the fact that previous authors have completely negated the familial aspect.

The appearance of myasthenia in infancy has been almost unknown until recently. The few cases cited did not always stand up to criticism. Accounts of myasthenia at the *foetal* stage have been published recently. LEVIN collected the cases found in literature with critical observations on the picture and progress of the disease. Also the account by GEDDES and KIDD as well as the most recent account by MACKEEVE. This seems to be the eleventh case in the literature. In the described cases signs of myasthenia appeared at birth, or within a few days after it. The newly born showed disturbances in swallowing and breathing, weak tongue and mouth motion, the face was without expression: In a few cases ptosis was noted, eyelid closing was incomplete, the muscular system weak and hypotonic. The subsequent fate of the new-born babies was not uniform. With a few the condition improved without the application of prostigmin. With others the symptoms disappeared with the use of prostigmin without reappearing after the medication was stopped, at least not during the period of observation.

In connection with signs of foetal myasthenia various questions of principal importance may be raised: what was the nature of the *substance* which was transferred from the mother to the foetus? How was it neutralised by the newly born? — for some of the children, after a stormy period in the beginning, were free of myasthenic manifestations without the help of prostigmin. What was the neutralisation mechanism that removed the neuro-muscular block? In experiments with animals thymus extracts of sufferers from myasthenia showed themselves free of the supposed curare like effect. Also the urine of myasthenic patients was inactive and did not produce a neuromuscular block. The same applies to blood injections. The investigations of LESNY stand isolated. After the injection of serum of myasthenic patients into guinea pigs he noticed ptosis, greatly accelerated tiredness and shortening of the swimming times. Injections of myasthenic serum together with prostigmin lengthened the swimming time and the symptoms of tiredness were lessened. It is questionable in how far experiments with only a few cases can solve such a complicated problem. The acetylcholine theory of neuro-muscular transmission is now generally accepted and proved through a great number of experimental facts. It has been proved that a nervous stimulus, which takes place without the production of acetylcholine does not cause muscular contraction. Acetylcholine depolarizes the membrances of the motor-end plate, and this depolarization is the specific factor which causes muscular contraction. The difference in potentials caused by depolarization can be registered.

According to the literature it has not yet been decided what is the cause of myasthenic symptoms, whether it is a lack of acetylcholine, or an accelerated disintegration, resulting from the increased effect of cholinesterase. The results of the examination of cholinesterase values in myasthenia are not unequivocal. The supposition that there is a want of acetylcholine with myasthenia has not been accepted. Addition of acetylcholine does not improve the symptoms. The therapeutic influence of prostigmin on the disease has been proved, although there are certain cases in which the effect is of very short duration and where even large quantities do not show good results. No binding conclusions are made — that myasthenia gravis is caused by a primary disturbance of the acetylcholine chemistry. The mechanism seems to lie much deeper, connected with the neuroendocrine system.

The role of the thymus in the pathological process is not yet clear, and in spite of a great deal of experimental work and therapeutic interference, the whole problem is still obscure. The successful results achieved by thymectomy are questioned by several authors.

The experiments with ACTH are still in the trial stage.

The therapeutic successes achieved by prostigmin and other cholinesterase hindering drugs have to be compared with and contrasted to the spontaneous remissions. Their number is not small. We report *M* in two children of a healthy mother which developed myasthenic symptoms at the same time. The clinical picture is similar to the cases described by LEVIN, and confirms, with small differences, the observations made there.

The mother of the sick children comes from a healthy family and has nine siblings who are healthy. Two of them, an older brother and a younger sister, were examined by us without showing any signs of myasthenia gravis. The mother — now twenty six years old — has always been healthy, except that she suffered in her youth from typhus. She works hard and does not complain of morbid tiredness. The neurologic examination shows a completely normal situation. X-ray examination of the mediastinum shows no pathological findings. The *first* pregnancy at the age of nineteen was completely normal, the weight of the male child was 3 500 g, the child screamed, cried and breathed normally. The child was nursed for eight months.

When the child was three months old, the mother noticed that the eyelids closed one or two hours after awakening and that they could be opened only with difficulty. After the midday nap the child kept its eyes open for about one hour to an hour and a half, and then they slowly closed; at night the child could not raise its eyelids. This situation persists to a varying extent to this day. At the age of two the child began to walk and to talk. Walking was good and improved quickly, talking was blurred and little articulated. Until the end of the third year the child could not chew and was dependent upon porridges and liquid foods. Solid foods were swallowed without being chewed, accompanied by frequent swallowing the wrong way. From the beginning of the fourth year chewing improved, but to this day it is connected with difficulties. During the meal the child has to support its lower jaw with its hand. It tends to catch cold. Mental development is slowed down. Being now seven years old the child attends school, but learns unsatisfactorily and unwillingly. He is irritable, anxious and timid. In recent years chewing has improved. The eyelids can be kept open well only in the morning and after sleeping and before noon they are already closed. Articulation is blurred, facial features are absent.

An examination of the child (Z. S.) shows the following: the eyelids are drooped and when looking straight forward they cover $^2/_3$ of the cornea. On attempting to

Fig. 1. Photographs of two brothers: showing ptosis, dropping jaw, sleepy expression and the open mouth.

look upwards the forehead is wrinkled and the head bent backward, closing of the eyelid is weak and after several closing motions strength clearly decreases. The pupils are equal, reaction to light and accommodation is good: ocular movements laterally and downwards are not limited; on looking upward there is tiredness after a few movements. The fundus is normal. There are no adenoid vegetations of the nasopharynx. The lower jaw drops, the mouth is held wide open. Closing of the mouth is possible but after ten or fifteen attempts the lips cannot be brought together. Lateral motions of the lower jaw easily become exhausted. Motions of the tongue are not disturbed. Uvula rises weakly at phonation, language is not distinct, gets tired by talking. Other neurological examinations give completely normal findings. The strength of the muscles of the nape, neck, the upper and the lower extremities is good, no tiring is noticeable. No atrophy of the musculature, myasthenic reaction was not found by electrical examination but the opposition of the child makes judgment difficult to a large extent. Reflexes of the upper and lower extremities are present but not increased. Rising from a horizontal position is quite free and so is walking and climbing.

Other findings: X-ray of the skull without pathological findings; ears, nose, mouth — normal; X-ray of the mediastinum without pathological findings; blood sedimentation rate $^{17}/_{26}$; erythrocytes 4 100 000 — leucocytes 6 400; urine: albumin sugar negative; blood Wassermann negative: creatinin 1.7 mg % — segm. 56, stab 4, lymph 34, mono 4, eos 2. The child was first seen by us when seven years old. The disease as described did not show progress in the course of time.

Under the influence of 0.35 mg prostigmin injections there was a definite improvement, after ten minutes ptosis improved, the improvement increased within the next fifteen minutes, eyelids were kept open, chin motions became free, mouth closing was strong. Chewing took place without difficulty, articulation improved, facial expression became lively. The whole behaviour of the child changed. This is clearly shown on the photographs taken before and after the prostigmin injection (see pictures). The influence of the medication was exhausted after more than two hours. Prostigmin taken orally three times daily in quantities of 0.015 mg improved the situation

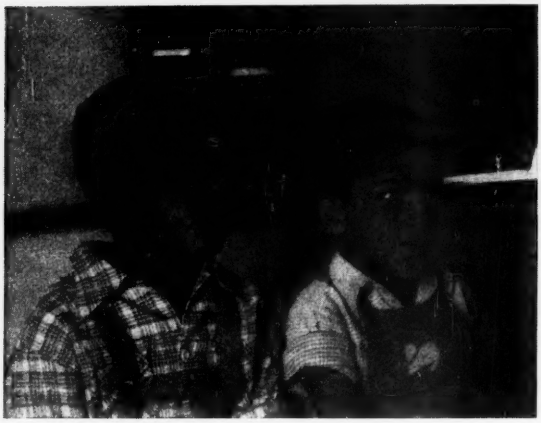

Fig. 2. Twenty minutes after injection of prostigmin 0.35 mg. Recovery of face activity.

but not to any great extent. Lessening of the ptosis was less obvious. Ephedrine in doses of 0.025 mg three times daily also was effective but it was badly tolerated and was stopped.

Three years later the second boy was born. The pregnancy was normal, foetal motions were felt until the end. The parturition was normal, the weight of the child 3 700 g, the child screamed and cried immediately after birth. In the third month the mother noticed almost the same phenomena as with the first child. Bilateral ptosis was present, which increased in strength in the course of the day, chewing and swallowing were difficult. To this day — the child is now five years old — it has to support its lower jaw while eating. Difficulties with chewing are more pronounced than with the brother, the mouth is kept open continually, articulation is slow and indistinct, the facial expression is tired and sleepy. In contrast with the brother mental development is good. Walking and running is unhindered. The tiredness mentioned above increases two hours after awaking and becomes stronger in the afternoon. The neurologic symptoms are limited to the eyelid, eye and chewing muscles. Ptosis is marked on both sides. Eye movements which are free in the beginning, become weak and restricted after several lateral movements. The same happens with upward motions, convergence takes place immediately, but after thirty to forty seconds the eyes cannot be kept in a convergent position; the lower jaw drops, is slightly raised and moves weakly to the sides. The mouth is not completely closed, pouting is almost impossible. Uvula movement is weak and tiring. The strength of the upper and lower extremities not diminished, reflexes are present, no atrophy. Walking and running is not limited. Other examinations: X-ray of the skull: no pathological findings; throat, nose, ears — normal; blood sedimentation rate: $^{30}/_{60}$. Hb 70 %. Erythrocytes: 3 500 000; leucocytes: 7 400, Wassermann, Kahn: negative. Urine: albumin and sugar — not found. Creatinin 1.4 mg%.

The prostigmin test with 0.35 mg subcutaneously showed a striking improvement up to the disappearance of the above mentioned symptoms. Fifteen minutes after the injection a clearly visible retraction of the upper lids took place which stimulated exophthalmos. The effect lasted for two hours, the face took on a lively expression,

closing of the mouth and chewing were freely executed. Oral administration of 0.15 mg prostigmin three times daily improved the situation without completely removing it. In the evening the phenomena of the disease were much more pronounced.

The clinical picture of the two brothers corresponds mostly with the observations made by LEVIN. The weakness affects the muscles supplied by the III, V, VII nerves. The weakness is symmetrical, the influence by prostigmin is unequivocal, the other bodily musculature is spared, at least at the time of the examination. It is difficult to foretell what course further development will take. At the moment the process is stationary, and small signs of some regression are noticeable with the older brother. Contrary to the report by LEVIN, the disease began, not immediately after birth, but, with both brothers at the age of 3 months. Fetal movements were felt by the mother throughout pregnancy. The children were born healthy and signs of myasthenia gravis were not noticed prior to the third month. We have, therefore, no reason to assume that the disease began prenatally. The cause why myasthenia gravis developed cannot be explained in our case, just as it could not be explained in the other cases.

Summary

A report is given of two cases — two children of a healthy mother — who acquired myasthenia. The disease appeared in both cases, in the third month of their life. At the age of five and seven years respectively, typical symptoms were present, affecting the eyelid, face and chewing muscles. Prostigmin improved the symptoms.

Myasthénie infantile grave familiale précoce.

Deux cas de myasthénie sont décrits chez 2 enfants issus d'une mère saine. La maladie apparut, dans les 2 cas, durant le 3^{e} mois de la vie. Les symptômes étaient typiques respectivement à l'âge de 5 et 7 ans. Ils intéressaient les paupières, la face et les muscles masticateurs. Amélioration symptomatique par la prostigmine.

Familiäre frühinfantile Myasthenia gravis.

Ein Bericht über 2 Fälle — 2 Kinder einer gesunden Mutter — die eine Myasthenie bekamen, wird gegeben. Die Krankheit trat in beiden Fällen im 3. Lebensmonat auf. Im Alter von 5 bzw. 7 Jahren waren die Symptome typisch ausgeprägt, betrafen das Augenlid, das Gesicht und die Kaumuskeln. Prostigmin besserte die Symptome.

Miastenia grave infantil familiar precoz.

Se describen 2 casos de miastenia adquirida en 2 niños hijos de madre sana. La enfermedad apareció en ambos casos al tercer mes de la vida. A la edad de 5 y 7 años respectivamente se manifestaban los síntomas típicos en los párpados, cara y músculos masticadores. El empleo de prostigmina hizo involucionar los síntomas.

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De l'Identité de la Maladie de Tay-Sachs et de Niemann-Pick

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Depuis que SACHS publia en 1887 une étude portant sur une famille présentant une dégénérescence cérébromaculaire, et chez laquelle TAY avait auparavant observé une tache rouge-cerise dans la région maculaire, on a cherché a plusieurs reprises à rapprocher cette maladie de Tay-Sachs (Idiotie infantile amaurotique) de la maladie de Niemann-Pick où dans plusieurs cas cette tache rouge-cerise a été retrouvée.

Nous croyons que l'histoire de la maladie de 2 enfants de la même famille pour l'un desquels nous avons porté le diagnostic de maladie de Tay-Sachs et pour l'autre celle de Niemann-Pick pourra peut-être éclaircir les rapports existants entre les deux maladies.

Premier cas: Le 24 Nov. 1949. H. D. une fillette âgée de deux mois, le troisième enfant d'une famille saine, est amenée à l'hôpital présentant un érythème fessier. Les parents, le frère et la sœur sont bien portants; la mère n'a jamais eu d'avortement. Cette fillette est née à terme, l'accouchement a été normal. Le premier mois elle fut nourrie au sein; après au biberon. Les selles et les vomissements seraient fréquents.

Status praesens: L'enfant ne parait pas très malade. Poids: 3200 g. La temp. est de 39°,5 C. Il y a une légère dyspnée, pas de cyanose. Le pharynx est rouge. L'auscultation pulmonaire révèle la présence de râles humides et secs assez gros, disséminés dans les deux hémithorax. Le cœur est normal. On note de plus de la séborrhée du cuir chevelu et un érythème fessier assez étendu. L'état de nutrition est satifaisant. La cutiréaction est négative. Rien de particulier dans l'urine. L'examen hématologique donne les résultats suivants: Hb. 10,4 g % (72 %), Er. 3,9 mill., Leucoc. 11 700 (Pol. neutr. 37, eos. 3, bas. 0, Lymphoc. 49, Monoc. 7, Plasmoc. 4.). Pas de cellules pathologiques.

L'enfant est réalimentée à l'aide de quantités croissantes de lait, additionné de sulfadiazine. Après 4 jours la température redevient normale et l'état des selles s'est amélioré. L'enfant est toujours enrhumée et tousse beaucoup; l'érythème est très varié. Peu à peu on aperçoit que le foie s'hypertrophie et que la rate est devenue palpable. Les ganglions cervicaux à peine palpables à l'entrée, ont maintenant la grosseur d'une

lentille. A la fin de Décembre la petite malade a toujours le même poids qu'à l'entrée. Le 3 janvier 1950 on constate un nystagmus horizontal, l'enfant s'occupe si peu de son entourage qu'on commence à douter de son intelligence.

La cuti-réaction répétée (Pirquet, Mantoux $^1/_{100}$) reste négative. La radiographie pulmonaire ne montre pas de lésions tuberculeuses. La réaction de Wassermann et celle de Meinicke sont négatives et ne changent pas après réactivation par un traitement au «spirocid». La ponction lombaire retire un liquide clair sous pression normale. (Trace de réaction de Pandy, réaction de Nonne négative, cellules $^7/_3$, réactions luétiques négatives).

L'examen ophthalmoscopique au début de Janvier (par le Dr. Hötte) donnait le résultat suivant: Papilles décolorées avec pourtour oedématié, aspect flou à gauche. Régions maculaires également oedématiées avec une assez-grande tache rouge-cerise sur la macula. A part cela rien de particulier même pas avec le microscope cornéen. Les pupilles réagissent bien à la lumière mais l'enfant ne suit pas des yeux un objet brillant qu'on déplace devant elle.

Evolution de la maladie: Au début de Février l'examen a été répeté avec le même résultat. Le 18 Janvier l'aspect était le suivant: enfant dystrophique, écoulement nasal non-diphthérique, légère hypertrophie ganglionnaire généralisée, au cou quelques ganglions de la grosseur d'une lentille. Le foie débordait de 3 travers de doigt le gril costal, la rate était nettement palpable. L'auscultation pulmonaire révelait la présence de gros râles disséminés. Erythème fessier avec pustules. L'examen hématologique à intervalles réguliers n'a rien révelé de particulier jusqu'ici.

Hémogramme du 15 Février: Hb. 11,5 g (80 %), Er. 3,6 mill., Leucoc. 15 800 (Polynucl. neutr. 40, eos. 6, bas. 1, Lymphoc. 41, Monoc. 12), Thromboc. 160 000. L'aggravation de l'état psychique devenait facile à remarquer. L'enfant ne saisissait plus l'objet avec lequel on lui touchait la main et ne manifestait aucun intérêt pour l'entourage; de temps en temps elle faisait des mouvements singuliers et incoordonés; en même temps les réflexes étaient dificiles à provoquer. Ainsi ce cas restait pour nous une énigme jusq'au 14 Février jour où nous trouvions pour la première fois dans le sang quelques grandes cellules singulières à structure vague.

Une ponction de la moelle osseuse faite après cette découverte donnait le résultat suivant: «Erythropoièse normale, leucopoièse normale, légère augmentation des réticulocytes. Il y a des cellules spumeuses typiques, comme on en trouve dans les lipoidoses.» Néanmoins les radiographies des os ne présentaient pas de particuliarités, les taux de cholesterine du sang était normal (98 mg %). Alors que le diagnostic semblait être fixé, l'état de l'enfant s'améliorait beaucoup. En quelques semaines son poids augmentait d'un kilo. Le 3 Mai à la demande des parents elle quitta l'hôpital dans un état assez satisfaisant quoique psychiquement retardée.

Le 15 Mai elle nous fut ramenée dans un état déplorable. Dépuis quelques jours elle avait des selles liquides et des vomissements fréquents. L'enfant présentait l'aspect typique de l'intoxication et mourait malgré des mesures appropriées. L'autopsie fut refusée.

En résumé: Une enfant saine a la naissance, issue d'une famille saine est amenée à l'hôpital à l'âge de 2 mois pour une dyspepsie accompagnée de fièvre. Dans les semaines qui suivirent la température devint normale et la dyspepsie disparut. On nota une hépatomégalie, une splénomégalie, des adénopathies cervicales et un changement de l'état psychique. Dans le sang on trouva des cellules spumeuses. Ceci joint à l'examen ophthalmologique montrant une tache rouge-cerise de la macula nous fit porter le diagnostic d'Idiotie Infantile de Tay-Sachs.

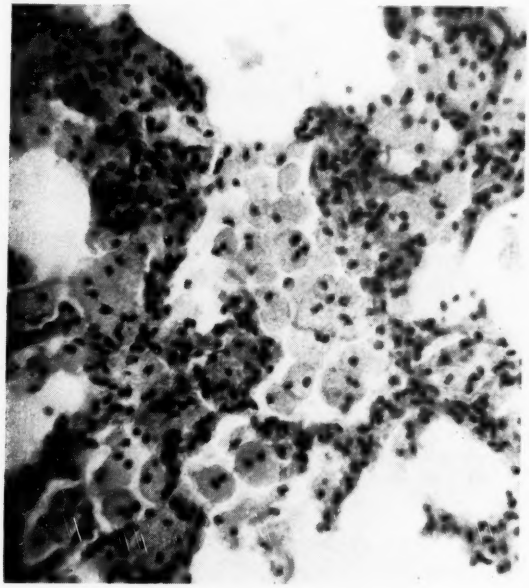

Fig. 1.

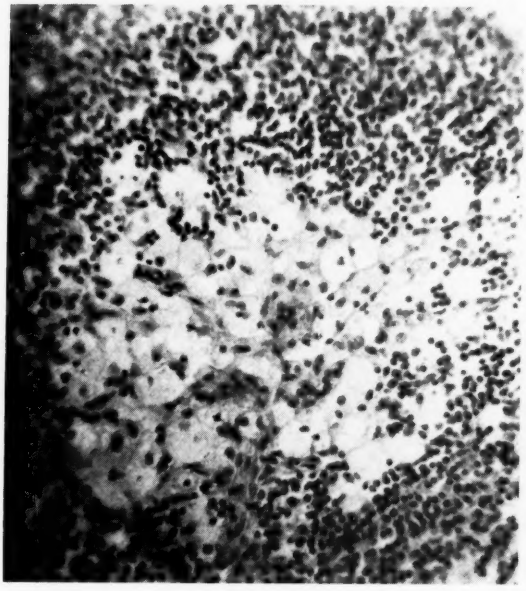

Fig. 2.

Deuxième cas: Le 22 Oct. 1951 à peu près un an et demi après la mort de la petite H. D. on nous amène son frère N. D. à l'âge de huit mois. L'accouchement avait été normal, l'enfant se développait d'un façon satisfaisant. Il y a une semaine il se mit à tousser et 3 jours après le médecin constatait une bronchite. L'enfant était très malade, cyanotique, avec battement des ailles du nez. Expiration prolongée, rétraction des côtes inférieures. Crâne hydrocéphalique (contour 50 cm). L'auscultation révélait des râles crépitants fins, prédominant en arrière. Le foie était hypertrophié étalant presque jusqu'a la crête iliaque de consistance dure et à bord lisse. La rate était également augmentée de volume et débordait de 4 travers de doigt le gril costal. Il n'y avait pas d'hypertrophie ganglionnaire. Les réactions à la tuberculine et de Wassermann étaient négatives. Hémoglobine 10,2 g % (70 % Sahli), Er. 3,5 mill., Leucoc. 57 600 (66 % lymphoc.). Temp. à l'entrée 39°,5 C. L'hématogramme nous faisait penser à la coqueluche, la culture du mucus trachéal était négative. Malgré des injections de pénicilline et de streptomycine la temp. continua à monter jusqu'a 41° C. L'hémoculture était négative; dans l'urine on ne trouvait rien sauf des traces d'albumine. Une ponction lombaire retirait un liquide clair sous une pression légèrement augmentée (cellules $^{7}/_{3}$, glucose 130 mg %). Le troisième jour après l'entrée l'état semblait s'améliorer quelque peu. La temp. baissait jusqu'a 39°,1 C, l'enfant paraissait un peu moins dyspnéique, le foie était beaucoup plus petit. L'examen du fond de l'œil ne révelait rien de particulier, mais la ponction de la moelle osseuse montrait quelques réticulocytes à structure spumeuse. Le quatrième jour après son admission et après une légère amélioration générale et locale, la température rémontait à 41° C et l'enfant mourait.

Autopsie: (par le Dr. H. v. d. Zalm) dont seulement les particuliarités les plus importantes sont indiquées ici:

Poumon gauche: Poids 70 g. L'arrière du lobe inférieur est parsemé de foyers pâles, durs et oblongs, qui sont plutôt palpables que visibles. Poumon droit: Poids 100 g. Même foyers qu'à gauche, mais localisés dans le lobe supérieur. *Rate:* Poids 70 g. Hypertrophiée à pulpe rose pâle, de consistance assez dure. Follicules visibles comme dans la rate «sagou». *Foie:* Poids 350 g. Assez grand et un peu dur, jaune pâle, homogène.

Microscopie: Poumons: Foyers circonscrits, pleins de lipoides. Les cellules épithéliales alvéolaires sont gonflées et changées en cellules spumeuses (Fig. 1). *Rate:* Les cellules de la pulpe sont presque toutes chargées de lipoides, causant un tel gonflement de la pulpe que les sinus sanguins ont l'air de petits canaux (Fig. 2). *Foie:* L'organe se compose à moitié de cellules hépatiques et à moitié de cellules spumeuses. Celles-ci se trouvent entre les cellules étoilées de Kupfer. *Glandes surrénales:* écorce normale, moelle pleine de cellules spumeuses. Dans le *cerveau*, le *thymus* et la *moelle osseuse* on trouve aussi des cellules spumeuses.

L'œil droit a été entièrement retiré et microscopisé. Les particuliarités telles qu'elles ont été décrites par SOMMER pour la maladie de Tay-Sachs n'ont pas été retrouvées ici.

Analyse chimique de la rate (par le Dr. E. Hollman): 31 % matière sèche, 69 % d'eau (total des lipoides de la rate 16 %, 52 % de la matière sèche). Le total des lipoides consistait en 26,8 % d'esters de la choline. Les lipoides purs consistaient en 2,5 mg % de N et de 1,06 % de P. La matière sèche était insoluble dans l'acétone et l'éther.

En Résumé: Garçon de 8 mois, dont la sœur est morte il y un an et demi d'une idiotie infantile amaurotique, est hospitalisé dans un état grave pour bronchopneumonie. A l'autopsie il apparait que l'enfant était atteint aussi de dyslipoïdose.

Discussion. De quelle nature sont ces lipoides? Les analyses chimiques dans notre deuxième cas permettent de conclure qu'il s'agit de la sphingomyéline et que le petit

garçon souffrait d'une maladie de Niemann-Pick. En ce qui concerne les symptomes cliniques, il faut bien se rappeler que probablement l'enfant est mort d'une infection intercurrente avant que sa dyslipoïdose ne se soit pleinement développée. Ainsi s'explique que le foie et la rate n'ont pas atteint le volume généralement décrit dans la maladie de Niemann-Pick ainsi que l'absence d'un nette atrophie. Bien qu'on ne pense plus, que la maladie de Niemann-Pick ne se développe exclusivement que chez les membres de la race juive, nous tenons à faire remarquer que le père des deux enfants est un enfant illégitime et que probablement le grand-père est polonais.

Restent enfin quelques rémarques sur les rapports entre les maladies de Niemann-Pick et de Tay-Sachs. SCHAFFER et son école opposent l'atteinte primaire des élements nerveux de l'ectoderme dans la maladie de Tay-Sachs à l'atteinte primaire du mésoderme dans la maladie de Niemann-Pick. PICK et BIELSCHOWSKI constatent cependant un rapport étroit entre les deux maladies. D'après leur opinion les phénomènes de dégénérescence du système nerveux central tels qu'on les voit dans la maladie de Tay-Sachs se retrouvent également dans celle de Niemann-Pick. Etant donné les résultats anatomopathologiques, microscopiques et chimiques de notre dernier malade le diagnostic de maladie de Niemann-Pick est certain. Il est evident que la maladie de la petite sœur est une lipoidose du même genre, quoiqu'on n'ait pas pu le constater par une autopsie. Pour la petite sœur cependant les phénomènes concernant le système nerveux central étaient beaucoup plus prononcés et les phénomènes ophthalmologiques étaient si nets qu'on a à juste titre pu porter le diagnostic de la maladie de Tay-Sachs.

Les recherches de KLERK qui dans la maladie de Tay-Sachs a trouvé une lipoide inconnue contenant du sucre qui, à l'analyse plus poussée contient un acide organique inconnu (l'acide neuramique) n'ont pas été encore confirmées. En considérant nos deux cas, nous croyons devoir aboutir à la même conclusion que VAN CREVELD (1): « Très probablement il s'agit dans ces deux maladies d'un même trouble métabolique lequel dans les tissus différents provoque les aspects de maladies différentes. »

Résumé

Se basant sur l'apparition du syndrome de Tay-Sachs et celui de Niemann-Pick chez deux enfants d'une même famille qui se succèdent, l'auteur en conclut que ces deux syndromes sont des manifestations différentes d'un même trouble du métabolisme lipoidique.

On the Identity of the Diseases of Tay-Sachs and Niemann-Pick.

Basing his opinion on the occurrence of the syndrome of Tay-Sachs and that of Niemann-Pick in two children, members of the same family and born of successive pregnancies, the author concludes that the two syndromes are different manifestations of the same disorder of lipoid metabolism.

Über die Identität des Morbus Tay-Sachs und Niemann-Pick.

Auf Grund des Auftretens der Syndrome von Tay-Sachs und Niemann-Pick bei zwei aufeinanderfolgenden Kindern der gleichen Familie schliesst der Autor, dass beide Syndrome verschiedene Ausdrucksformen der gleichen Störung im Lipoidstoffwechsel sind.

Sobre la identidad de la enfermedad de Tay-Sachs y Niemann-Pick.

Basándose en la aparición del síndrome de Tay-Sachs y el de Niemann-Pick en dos niños de una misma familia, que se sucedieron, el autor saca la conclusión de que estos dos síndromes son manifestaciones diferentes de un mismo menoscabo del metabolismo lipoide.

Reference

1. S. VAN CREVELD dans L. PARSONS: Modern Trends in Pediatrics, 1951, où on trouve également une bibliographie très étendue des lipoidoses.

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Pattern of Children's Disease and Death as Seen in a Children's Hospital, Colombo, Ceylon

by C. DE SILVA, O. C. RAFFEL, and PRIYANI SOYSA

For the purposes of this paper we have analysed the admissions to our unit from 1/10 1950 to 30/9 1951, 2 168 in all and aged from birth to 13 years. We have also analysed the admissions to the Surgical Ward under the Professor of Surgery during 1950—1951 and shown these separately.

Medical cases

A statistical analysis of our figures shows no preponderance of males over females as has been shown by workers of other countries (TISDALL, 1930; POULTON, 1950).

There were 3 446 illnesses in the 2 168 admissions, i.e. 1.5 illnesses per admission. More than one admission in the same patient during the period under review has been counted as separate admissions. No children suffering from any infectious fevers or skin diseases were admitted to our unit.

Chart 1 shows on the left hand clear bar the number of cases of all diseases at various age periods — and on the right hand black bar the number of deaths at corresponding periods.

The period 1—2 years had the largest number of cases of any age period of one year. The over 5 year period was a composite one containing cases from 8 separate years. This increase in the 1—2 year period was statistically significant[1] as compared to all other single year periods. What was unexpected was that it was a larger group than the 0—1 year period and that this

[1] The test of significance employed in this and all other instances was

$$t = \frac{p1 - p2}{\sqrt{\frac{p1\,q1}{n1} + \frac{p2\,q2}{n2}}}$$

where $p1$ is the percentage or rate in the first sample and $p2$ is the second sample.

The level of significance adopted in all statistical analyses of this paper is P 5 %.

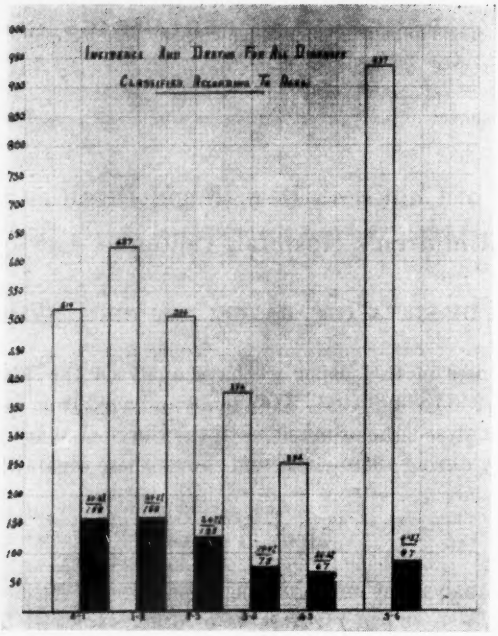

Chart 1. Incidence and deaths for all diseases classified according to ages.

increase was statistically significant. This was, we believe, due to the great increase in the incidence of intestinal parasites and nutritional disorders which more than balanced the decrease of respiratory and nervous disease at this age (see Chart 7).

Though the incidence was greatest at this age the fatality rate was, as expected, higher in the 0—1 year period (30.4 % against 25.2 % in the 1—2 year period). Though the over 5 year period contained the largest number of cases, it showed at the same the lowest fatality rate, which was significantly less than the rates for each of the preceding years.

Fatality rates. The fatality rates were very high. There were 496 deaths: 232 or 46.7 % occurred within 24 hours and 271 or 54.7 % within 48 hours of admission. If we excluded the deaths within the first 24 hours then our fatality rate was 12.1 %, and if those within the first 48 hours were omitted then this rate was reduced to 10.3 %.

These figures were still high. They were due to:

1. The very poor nutritional status in the children of the hospital classes. The average red blood cell count in 461 children in the hospital was 2.6 million per c.mm and the average haemoglobin was 8.6 g % (DE SILVA, 1951).

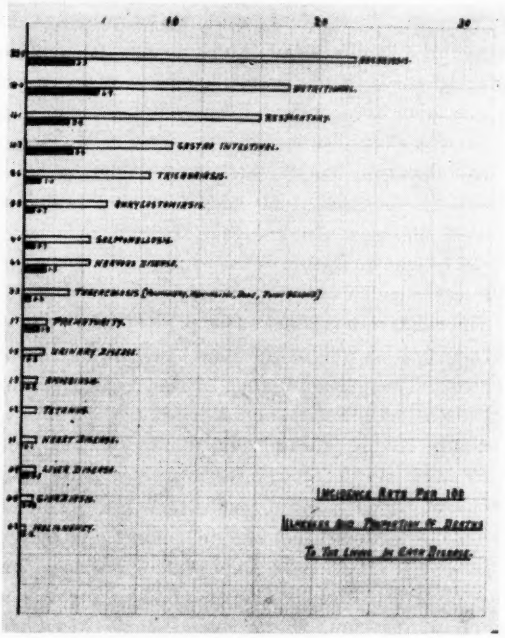

Chart 2. Incidence rate for all diseases per 100 illnesses and proportion of cases living to dead in each illness.

2. 62.9 % of over 1 700 individual cases in hospital showed the presence of intestinal parasites. Severe infestations were very common.

3. Serious neglect of the elementary rules of sanitation and hygiene was usual in the previous history and management of the children.

4. There is a severe shortage of nursing and medical personnel.

SMELLIE's figures (1949) for fatality rates in infants at the Birmingham Children's Hospital were as follows:

TABLE 1

Comparison of infected and non-infected cases from Children's Hospital, Birmingham (SMELLIE 1949) and the present series and the fatality rates of each. Infants under 1 year of age.

	Infected cases	Fatality rates %	Non-infected rates	Fatality rates %	Infected to total cases %
SMELLIE . . .	904	17.3	1 402	15.7	39.2
DE SILVA . . .	487	31.1 (No = 151)	35	20	93.2

In SMELLIE's series of 2 306 infants under 1 year of age 39.2 % were infected. In our series of 522 infants of the same age, 93.2 % were infected.

Of the 487 infected cases in our series 322 were cases of preventable disorders (66.1 %), i.e. diarrhoea, intestinal parasites, tuberculosis and nutritional disorders. In SMELLIE's series of 904 cases, there were 313 probable cases of preventable illnesses, 34.6 %, i.e. just over half ours.

On an analysis of all illnesses at all ages admitted under us 74.5 % were cases of preventable diseases. An analysis of TISDALL's cases (1930) from Toronto showed 28.7 % as probably preventable, i.e. we have 2 $^1/_2$ times as many preventable cases as Toronto.

Chart 2 shows the relative incidence rates per 100 of all the common conditions met with in our unit as well as (in black) the proportion of deaths to the living in each disease. The predominance of the Ascaris lumbricoides as the commonest disorder of childhood should be noted. We have labelled the Ascaris, Public enemy No. I. of childhood in Ceylon. The nutritional group took second place and respiratory infections the third. Gastro-intestinal diseases were less common than the respiratory but all intestinal parasitic disorders have been shown separately and not included in the gastro-intestinal diseases. The Trichuris trichiura was a commoner parasite than the Necator americanus. The relatively high incidence of salmonellosis was surprising.

For purposes of comparison, the corresponding figures from TISDALL's series from Toronto are shown on the same scale as ours (Chart 3).

From the charts it is obvious that the disease pattern in the two materials is very different, the only exception being the respiratory diseases which are comparatively frequent in both. A few comments on some of the other diseases are warranted.

Endocarditis which was the commonest cause in TISDALL's series was negligible in ours. What has been labelled as heart disease in ours, and was the fourth from the bottom, contained 29 cases of congenital hearts to only 10 cases of rheumatic carditis. Scarlet fever is non-existent in India and Ceylon. Chorea was fifth in TISDALL's series. We had only two cases of chorea during the period under review and these were included under nervous diseases. This is an uncommon disorder in the tropics. Epileptics were rarely admitted but treated in the out-patient department. There were only 6 cases treated as in-patients in the hospital.

The rate of incidence of intussusception in our series (0.44/100) was one tenth the rate of the Canadian series. Pyloric stenosis was 1/13 (0.30/100) and there was only one case of appendicitis per year. These low rates were probably due to patients not seeking hospital treatment due to a dread of surgery and seeking instead the aid of practitioners of indigenous medicine.

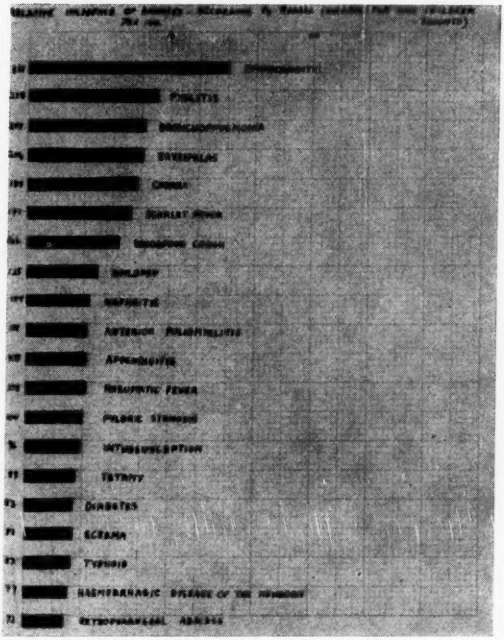

Chart 3. Incidence rate for all diseases per 100 illnesses as seen at the Hospital for sick Children. Toronto, Canada. (TISDALL, 1930.)

Surgical cases

The relative incidence of surgical cases admitted during 1950—51 as shown in Chart 4 was on the same scale as the medical cases.

The congenital abnormalities constituted a large group of all illnesses — medical and surgical. The incidence of infective cases i.e. abscesses, cellulitis etc. was also very high. Poisoning was mainly caused by kerosene oil, and trauma was due more often to burns than to accidents.

Chart 5 shows the incidence of each individual congenital abnormality as seen in the surgical unit. (The congenital hearts as seen in the medical unit have also been included in this chart — on the same scale and calculated as the incidence rate for two years). The marked preponderance of harelips and cleft palates should be noted — an incidence of over 30/100. Congenital herniae were the next commonest and congenital hearts the third. Imperforate ani were not rare. Pyloric stenosis was less common than imperforate anus but this may have been due to the fact that while every case of the latter was referred to hospital, many cases of the former were probably treated by qualified as well as unqualified medical practitioners.

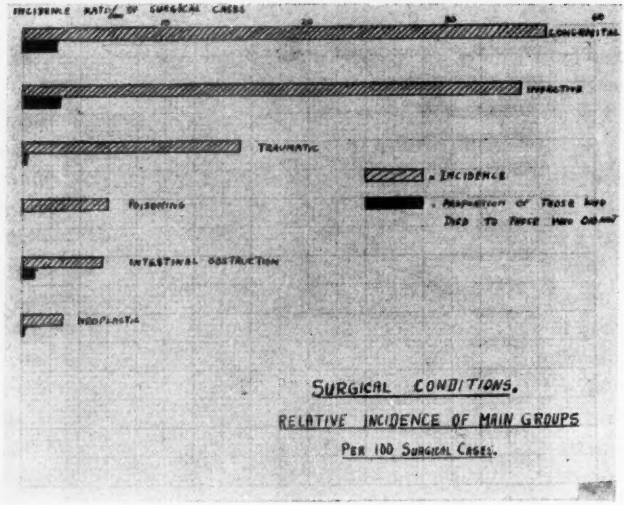

Chart 4. *Surgical cases.* Incidence of each main group of illness per 100 and proportion of cases living to dead in each group.

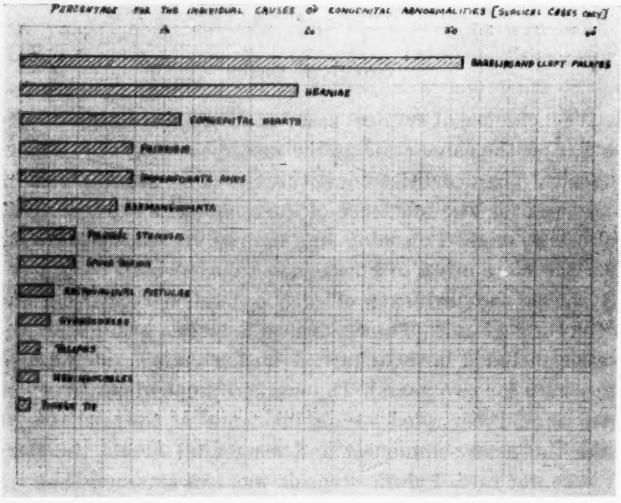

Chart 5. *Surgical cases.* Incidence rate of each congenital condition per 100.

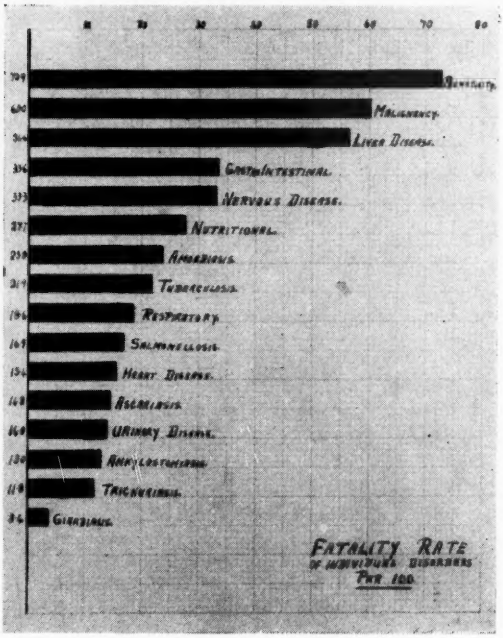

Chart 6. Fatality rate of individual disorders *per 100*.

Fatality rates of each disease

Prematurity headed the list of fatality rates (Chart 6). That was due to the fact that most of the prematures that were admitted to the Children's Hospital were ill either with a gastro-enteritis or a respiratory infection and very rarely were they seen without some pathological disorder. Further, there was no special premature unit for isolation nor personnel specially trained for nursing these infants.

The malignant group which comprised only 17 patients, included cases of acute leucaemia, Hodgkin's disease, Wilm's tumour, cerebral tumour, neuroblastoma and hepatoblastoma.

Liver disease excluded all fatty livers (these were included under nutritional disorders) and included cirrhosis and infective hepatitis. En passant, it may be stated that though infantile biliary cirrhosis did occur in Ceylonese, it was much less common than in South India.

Of the intestinal parasites, amoebiasis had a higher fatality rate than any of the helminths. A large number of children had both infections, and some cases of amoebiasis were admitted at a very late stage. Three autopsies on these

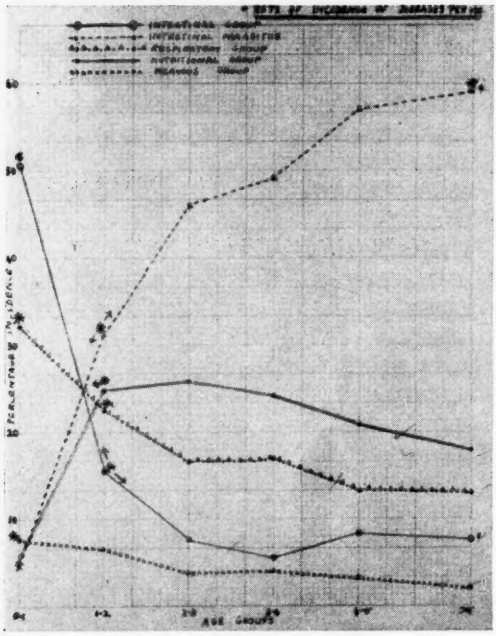

Chart 7. Incidence rate of the 5 main groups of illnesses as seen in the medical wards. a) Intestinal parasites. b) Nutritional group. c) Respiratory group. d) Gastro-intestinal group. e) Nervous group.

cases revealed an advanced degree of ulcerative colitis. Of the diseases due to helminths, ascariasis had a higher fatality rate than any of the others while ancylostomiasis took second place.

Gastro-intestinal disorders had a fatality rate of 33.6 %. — The fatality rate of nervous disorders was also 1 in 3. This was due to the high incidence of febrile convulsions which had to be included under this heading because in several cases the cause was unknown. Nutritional disorders had a fatality rate of 27.7 %. Many of these have shown the Kwashiorkor syndrome. Tuberculosis has lost just over 1 in 5 (21.9 %).

Classification of diseases

All the cases admitted to our unit have been classified into 5 main groups for the sake of simplicity:

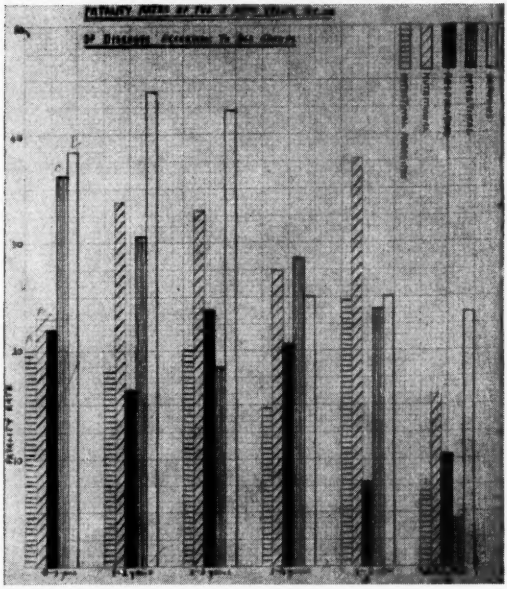

Chart 8. Fatality rates of the 5 main groups per 100 of diseases according to age groups.

1. Intestinal parasites	1 332 cases
2. Nutritional disorders	683 cases
3. Respiratory diseases	613 cases
4. Gastro-intestinal disorders (excluding intestinal parasites and amoebiasis)	510 cases
5. Nervous disorders	159 cases
	3 297

There was a discrepancy of 149 cases. These were accounted for by (1) Liver diseases — 29 cases; (2) Kidney diseases — 49; (3) Diphtheria — 17 (only cases needing tracheotomies were admitted); (4) Hearts — 39; (5) Malignant diseases — 10 (not including 7 from the surgical ward); (6) Congenital syphilis — 5.

Chart 7 shows the incidence of each group of diseases at each age period. The asterisks on this chart showed the statistically significant points.

The fatality rates for the 5 main groups and the various age groups are evident from Chart 8. The statistically significant points are again marked by asterisks.

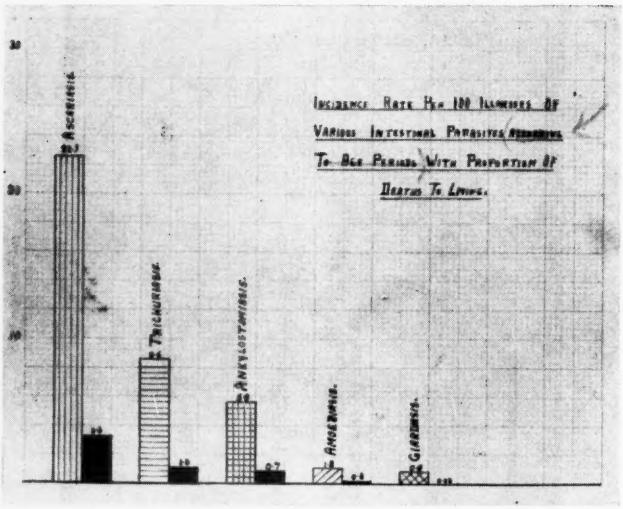

Chart 9. Incidence Rate per 100 illnesses of various intestinal parasites with proportion of deaths to living.

Intestinal parasites

There were 1 332 cases of intestinal parasites and their relative incidence is shown in Chart 9. This chart demonstrated the dominant role of the ascaris in the ranks of intestinal parasites. The cases of ascaris were further analysed in Table 2.

TABLE 2

Classification of cases of ascariasis into 3 main groups with the incidence and fatality rates of each.

Type	No. of cases	% of total	No. of deaths	Fatality rate
1. Alimentary	269	35.5	32	11.8
2. Toxaemic	144	18.9	40	27.7
3. Incidental	346	45.6	43	12.2
	759	100.0	115	15.0

We have classified our 759 cases of ascariasis into 3 main groups:

1. *Alimentary.* These included all cases of diarrhoea and vomiting, abdominal pain or colic, dyspepsia, anorexia or pica for which no other cause could be found and in which adult ascarides or ova were passed in the stools.

2. *Toxaemic.* These were characterised by a high temperature, restlessness, irritability, grimacing or on the other hand, drowsiness, stupor, semi-coma or coma. Often,

though not always, convulsions were also present. The abdomen was full and tense and the round worms could be felt on light palpation with the flat of the palm. The fatality rate of this group was more than twice that of either of the other groups and was found to be statistically higher in comparison not only to the fatality rates of each of the others but also to the total fatality rate of all cases of ascariasis.

3. The last group was the incidental one where the child was admitted for some other concomitant illness and found to be harbouring the ascaris worm.

The second commonest intestinal parasite was not the Necator americanus as was expected but the Trichuris trichiura. This parasite was pathogenic to our malnourished children especially when there was a heavy infestation. This was manifested by a chronic diarrhoea very resistant to treatment and the stools often contained blood, pus and mucus. Repeated examination of the faeces has shown no other parasite and cultures have been negative for salmonellae, shigellae and entamoebae histolyticae.

The typical clinical picture of severe infestation with the Necator americanus is common and has by no means been eradicated from among the preventable diseases of childhood.

The entamoeba histolytica was responsible for 8.2 % of all diarrhoeas including salmonellosis but excluding those due to intestinal parasites. This was a significant proportion and much higher than that given in the usual text-books. The Giardia lamblia was responsible for 29 cases. We were certain that where there was a heavy infection, especially with the trophozoite, it was pathogenic to children. Other rare occurrences were Strongyloides stercoralis (4), Hymenolepis diminuta (3), and Balantidium coli (1).

Nutritional disorders

The second largest group was the nutritional one. This comprised 683 illnesses (or 19.8 per 100). If we excluded 59 cases of prematurity we were left with 624 nutritional disorders (or 18.0/100 illnesses).

There was a significant rise in the incidence of nutritional disorders at 1—2 year age period and a slight, statistically insignificant rise from 1—2 years to 2—3 years. After that there was a gradual fall which was not statistically significant at any point (Chart 7).

The nutritional disorders forming a total of 683 cases included 166 cases each of fatty liver and oedema, and 123 cases of Vitamin A and riboflavin deficiencies of the eye (i.e. xeropthalmia, Bitot's spots and keratomalacia). Most of our cases of malnutrition showed these changes. Apart from the above mentioned ophthalmological signs there were two conditions that must be stressed because these have not been reported earlier by any workers to our knowledge and in Ceylon they have not been included as stigmata of deficiencies in nutritional surveys:

Fig. 1. Diagrammatic illustration of a pre-Bitot pigmentation.

Fig. 2. Diagrammatic illustration of a "gutter" pigmentation.

1. A dirty brown pigment of the sclera is present extending in band-like form from the edge of the cornea horizontally to the periphery or sometimes in the shape of a triangle with its base centrally and apex peripherally. Xerophthalmia is always associated with this sign. Often, though not always, the Bitot spots have appeared near the base of the triangle. We have named this a pre-Bitot pigmentation to distinguish it from a Bitot's and also to emphasize the fact that we have noted clinically that a Bitot often started within a pre-Bitot. This Bitot, however, also appeared independently and without the prior presence of the pre-Bitot (Fig. 1).

2. If one pulled the lower lid down there was often in our children a band of pigment at the lower margin of the bulbar sclera where it joined the palpebral sclera. Sometimes this pigment overflowed on to the lid itself. We have called this a "gutter" pigmentation. This pigment varied from the lightest of light brown with a general fading towards the upper margin to a very dark, dirty brown with involvement of the lower part of the palpebral conjunctiva. Trachoma is a rare condition in Ceylon and these cases are not trachomatous — so I am informed by an ophthalmologist who has seen many cases of trachoma and "gutter" pigmentation in Ceylon (Fig. 2).

Vitamin A by itself in large doses (50 000—100 000 units) injected intramuscularly several times had no effect on this gutter pigmentation. Riboflavin (mg 1) parenterally by itself has had no effect. The combination of the two continued for a long time at weekly, bi-weekly or daily intervals, did often resolve the lesions but not invariably so. This was probably due to the fact that the patients did not continue treatment long enough. In one case it took over 8 weeks for this pigmentation to disappear.

Kwashiorkor was fairly commonly seen but our cases were very often complicated by vitamin A and riboflavin deficiencies as described above.

The characteristic "crazy pavement"[1] rash of Kwashiorkor which commenced most commonly round the perianal region originated in two different ways:

1. Areas of hyperpigmentation coalesced and became larger and then desquamated leaving now hypopigmented layers of epidermis underneath. This type did not cause a high mortality.

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[1] We think that this term is misleading and confusing as the same term is used to describe mosaic skin dermatosis of the limbs as well. Dr. Cecily Williams who first named this "crazy pavement" agrees in a personal communication to the author to change the name to a "peeling pellagroid" rash which is a much more satisfactory term.

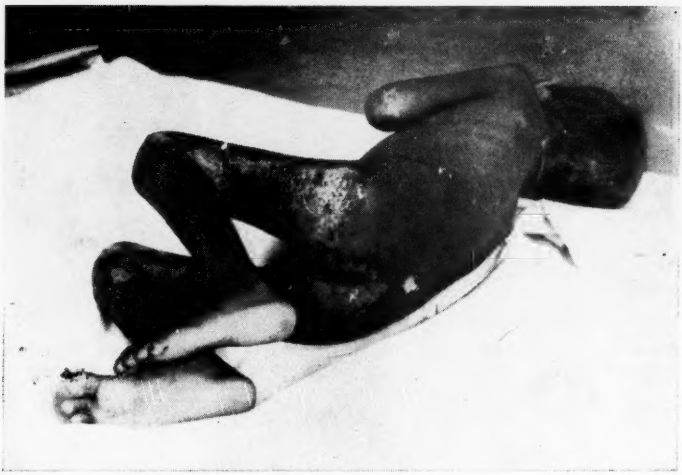

Fig. 3. Shows the hyper-hypopigmented rash particularly in the perianal and gluteral regions and down the lower limbs.

2. A second type which commenced as small petechial haemorrhages which coalesced and formed larger patches of a dirty plum-coloured rash which desquamated and left raw, red weeping areas of dermis underneath with no new epidermis. These areas often got infected and the prognosis was usually grave in the condition. Has vitamin C deficiency anything to do with this? Published work on Kwashiorkor has not laid much stress on avitaminosis C as the cause of this type of rash. We are at present undertaking some research into this problem.

Kwashiorkor or malignant malnutrition has been described by several writers in different parts of the world. — The most recent publications were a series of three papers from Kampala, Uganda (DEAN 1952: TROWELL and DAVIES 1952 and TROWELL, DAVIES, and DEAN — 1952) and one from Coonoor by VENKATACHALAM *et al.* — 1952. We had 30 cases in this series that answered to the description namely with oedema, enlarged liver, anaemia and skin rashes of the 2 types already mentioned — Figure 3 shows one hyper-hypopigmented rash which commenced round the anus and extended down the legs and gluteal regions. Before the hypopigmented patches peeled off the underlying skin had grown the new epidermis which was less pigmented than normal.

Figure 4 shows the picture of a child with a rash that started as petechial haemorrhages which then coalesced to form hyperpigmented areas of varying sizes. — These peeled off leaving raw red surfaces oozing serum underneath. These were usually infected; the prognosis was grave in this type of case.

The average age in our cases was 2 years and 4 months. — The range lay between 10 months and 8 years.

Fig. 4. Show the rash which often started as petechial haemorrhages. This case manifested a wider distribution than usual. She also had clear cut ulcers.

	Incidence	Deaths
Under 1 year	1	1
1 year —2 years	19	6
2 years—3 years	6	3
3 years—4 years	3	3
4 years—5 years	2	2
5 years—6 years	—	—
6 years—7 years	—	—
7 years—8 years	1	—

Fifteen of the 30 cases died. Five died within 24 hours of admission and the average duration of illness for all the cases was 52 days ranging from 5 to 120 days. Twelve of the 15 deaths occurred on those children who had been ill between 1—2 months.

The average weight was 14 lbs. 3 ozs. — The weight was grossly deficient (over 20 %) in the great majority of cases. The blood showed usually a macrocytic, slightly hypochromic type of anaemia. The average haemoglobin was 5.9 g % (Sahli) ranging from 2.8 to 11.6 g %. The average red blood corpuscle count was 2.212 000 per c.mm and it ranged from 1.020 000 to 3.440 000 per c.mm. The cases were too few to draw definite conclusions but the red blood corpuscular and haemoglobin levels had apparently very little to do with the ultimate prognosis. The liver was not enlarged in 14 cases — 3 cases each showed enlargement to 1, 2, and 3 fingerbreadths respectively. There was no record in 7 cases.

The larger the liver the better the prognosis. This was shown not only in this but in a larger series. A few liver biopses were done which showed the intense fatty infiltration of all liver cells but the size of the liver globule varied — in some forming what has been described as fatty cysts — due to the coalescence of adjacent fatty globules. We do not agree that the fatty change is always most intense and advanced in the periphery of the lobule. We have seen post mortem specimens where the fatty changes have been most marked in the mid-zone or in the central part of the lobule. — The reasons for this difference in the histological appearances in different cases exhibiting very similar symptoms are obscure. In 2 cases in which we were able to do autopsies soon after death the histological appearances of the pancreas were reported as normal.

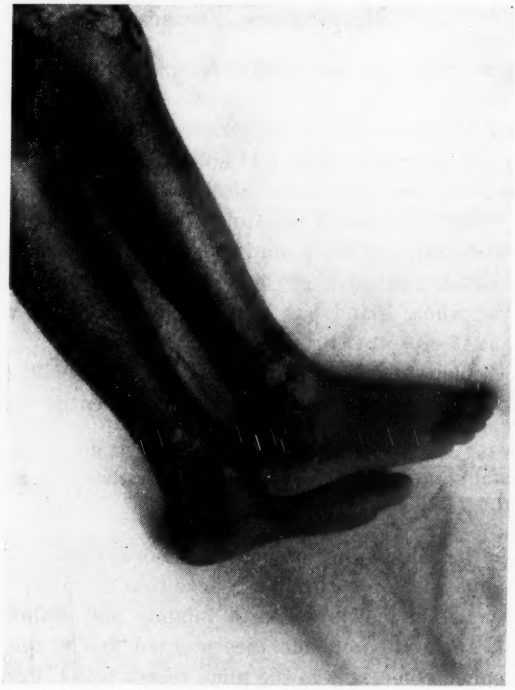

Fig. 5. Shows a combination of a mosaic skin dermatosis together with hypo-hyperpigmented rash on the lower limbs.

In nearly all cases there was some degree of oedema present — sometimes only of the hands and feet. The oedema started most commonly in the lower limbs. Most of the cases showing oedema also manifested ascites. A few cases showed lack of elasticity of the skin of the abdomen (or dehydration), at the same time as there was oedema of the lower limbs. The explanation for this living paradox was also obscure. Vitamin A and riboflavin deficiencies were present in nearly every case.

Most of the cases also showed infestation with intestinal parasites and particularly with the round and the whip worm. Scanty, brown, brittle hair was seen in the majority of the cases. The colour of the hair was much lighter than in normal children of the same age, class and community. The dietetic history in slightly over half of the cases (16) showed prolonged breast feeding, i.e. over 6 months — in 8 cases over 1 year and in one case over 2 years. Once the breast milk failed only rice and vegetables were given. — In a minority of cases inadequate quantities of dried or cow's milk were also given. In some patients dried sprats or fresh fish or lentils were given occasionally.

Since 1951 the fatality rates have been reduced by feeding the children suffering from Kwashiorkor with skim milk and by treatment with blood transfusions.

There were 10 cases of rickets and 4 of scurvy — all radiological diagnoses — during this period.

Respiratory diseases

The third largest group was composed of respiratory illnesses. These totalled 613 (17.7/100).

The incidence of respiratory disease decreased significantly from 1—3 years (Chart 7) but after that there was no significant variation. This group included 73 cases of pulmonary tuberculosis — 24 primary, 43 postprimary and 6 miliary. There were also 8 cases of tuberculous meningitis during the same period. Tuberculosis of the pulmonary and meningitic types comprised 81 cases. The mortality rate per 100 000 of the population from tuberculous meningitis in the whole island has increased by 115 % between the years 1936—40 and 1945—49 (DE SILVA, 1951).

The non-tuberculous respiratory diseases totalled 540 illnesses (15.6/100) — Bronchopneumonia 218 (6.3 per 100) with 71 deaths (fatality 32.5 %).

Under 5 years 197 cases — 69 deaths — fatality rate 35.0 %. Over 5 years 21 cases — 2 deaths — fatality rate 9.5 % over two-thirds of the deaths occurred in the group under 2 years (67.6 %).

In contrast to the 218 cases of bronchopneumonia there were only 23 cases of lobar pneumonia with 3 deaths. We believe that the older view that bronchopneumonia was much commoner in infancy and childhood was quite correct and this apparent preponderance was not due to the higher fatality rate of bronchopneumonia as was the more recent belief. Further, where we have X-rayed these patients, we have found apical lobar pneumonia to be as common as the basal affection.

There were 8 cases of lung abscess usually post-pneumonic, with 1 death. None of the cases had surgical treatment. The commonest organism isolated from cough swabs was the B. Friedländer.

Gastro-intestinal disorders

There were 510 cases of gastro-intestinal diseases (14.8/100). The morbidity rate at the 0—1 year period was significantly higher than at all other periods and the rate at the 1—2 year period was significantly higher than at all older periods. Beyond 2 years there was a flattening out of the curve showing a more or less equal incidence rate in each subsequent year (Chart 7).

The fatality rates were extremely high for the whole group — 33.6 % of the children died, i.e. 1 in 3. Under 2 years — 37.1 % fatalities and over 2 years — 25.0 %.

But this does not give a true picture of the severity of diarrhoea as seen in the city and its environs because we only admit cases (1) with dehydration, (2) with high temperatures or other signs of toxaemia, (3) with a history of

TABLE 3

Salmonellosis.

The high incidence and fatality rates of infections due to S. virchow and S. adelaide in the younger age groups contrasted with infections due to S. typhi.

Ages	Cases due to S. typhi	% Cases of S. typhi to total	Deaths from S. typhi No.	Cases of Salmonellosis (other than those due to S. typhi)	% of Salmonellosis to total Salmonellosis other than S. typhi	Deaths No.	Fatality rate of Salmonellosis other than from S. typhi		Totalfatality rate, all Salmonellosis including S. typhi	
0—1	0	0	0	45	39	14	31		31	
1—2	2	4	0	22	19	7	32		29	
2—3	1	2	0	16	14	2	12		12	
3—4	3	7	1	5	4	0	0	60	12	50
4—5	9	21	1	4	3	2	50		23	
> 5	29	66	0	24	21	0	0		0	
	44	100.0	2	116	100.0	25	21		17	

a very chronic or recurrent diarrhoea of over 2—3 months duration, (4) with blood in the faeces. Therefore, our fatality rates are bound to be exaggerated — especially, as approximately half the deaths occurred within 24 hours of admission.

Three hundred and fifty of these cases of gastro-intestinal diseases were due to undiscovered causes.

Samples of faeces from all cases of diarrhoeas in our ward were sent for culture of dysenteric organisms and salmonellae. For nearly 2 years particularly in the neonatal period, stools have been investigated for E. coli var. neapolitanum $\alpha + \beta$ types with almost completely negative results to date. One β type and one unknown type were found in two separate cases from the Children's Hospital but none at the Maternity Hospital. The unknown type is at present under investigation at the International Salmonella and Escherichia Centre, Copenhagen (SCHMID 1951). One infant's (aged 3 days) stools from the Maternity Hospital cultured a S. adelaide. This is the youngest case on record in the literature to have isolated a salmonella. There was a very high incidence of salmonellosis in the children's hospital — 160 cases, of which only 44 were due to S. typhi. The all-over incidence is 4.6 per 100 illnesses (Chart 2) i.e. 460/10.000 in contrast to KAUFFMANN's (1941) figures of 8.3/10.000. Salmonellosis is the seventh commonest condition found in our unit. SCHMID and VELAUDAPILLAI (1951) have done a survey of salmonellosis in Ceylon. They have found 26.9 % of diarrhoeal stools sent from the Children's Hospital, Colombo, between July 1950 to February 1952 positive for salmonellae. The commonest types found were S. adelaide 70.1 % and S. virchow 23 %. Table 3 shows the high incidence of S. adelaide and virchow in infancy and its diminishing importance as age advanced in contrast to the absence of S. typhi under 1 year and its increasing importance as the child grew older. It also showed the high fatality rate in infancy and early childhood and its reduction later on with a total absence of deaths over 5 years.

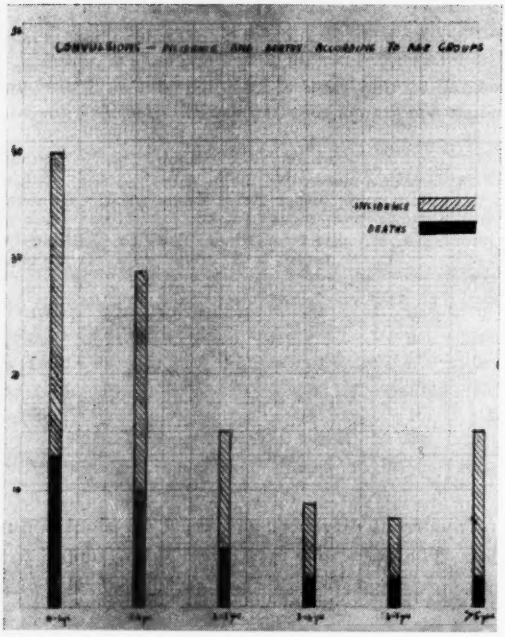

Chart. 10. Convulsions — incidence and deaths according to age groups.

Nervous disorders

The last group that we must consider was that due to nervous disorders. These showed a total of 159 cases (4.8/100). There was a significant increase in the 0—1 year period as compared to the rest. The incidence and the fatality rates under 3 years were significantly higher than those over 3 years. Considering that the total number of cases of all illnesses was higher in the 1—2 year period, the incidence rate for convulsions in the 0—1 year age period was much higher than in any other period as seen in Chart 10. This chart also showed that the deaths were significantly higher in the 0—1 year period.

Chart 11 shows the causes of febrile and non-febrile convulsions in 104 cases of the former as well as the number of deaths from each condition and 10 cases of the latter. Bronchopneumonia was the commonest cause in the former and birth injury in the latter. In a large number of cases the cause could not be discovered owing to the death of the patient within a few hours of admission and denial of permission for an autopsy.

There were 58 cases of tetanus both in the surgical and medical units. The incidence rate of 1.2/100 is considerable. We have seen only 4 cases of tetanus

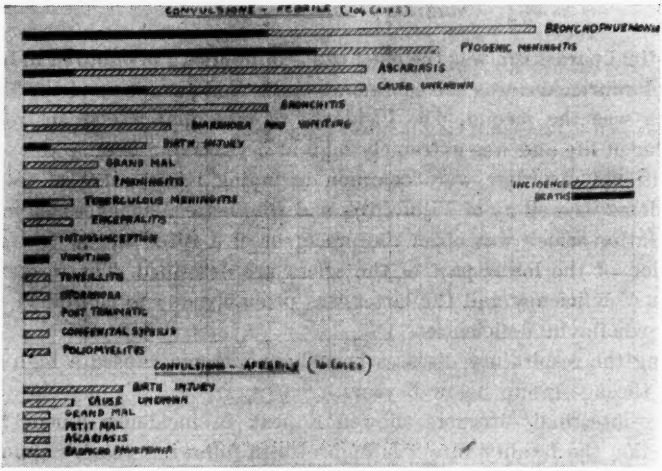

Chart 11. Causes of Febrile and non febrile convulsions with deaths due to each cause in black.

neonatorum in the last three years but in 1932 before the midwives ordinance became law, one of us (C. C. de S.) saw three cases in one month in general practice. Nearly half the total births in Ceylon are now attended by registered trained midwives. The reduction in the number of cases of tetanus neonatorum is due to the gradual but sure elimination of the untrained midwife.

There were 24 cases of pyogenic meningitis with the highest incidence under 1 year (9 cases). There were 13 deaths — fatality rate of 54.2 %. The fatality rate was in inverse ratio to the age. The commonest organism isolated was the H. influenzae. A full analysis of pyogenic meningitis from our unit has been published by FERNANDO and DE SILVA (1951).

We had 8 cases of tuberculous meningitis during this period of which only one was over the age of 3 years. They were all fatal. A full review of all our cases from 1949 onwards has been published by HAMZA and DE SILVA (1951).

There were 29 cases of poliomyelitis with 8 deaths. In the period under review we had a high incidence of bulbar and cervical cases. These carried a higher mortality. The incidence of poliomyelitis was highest during and after the monsoonal rains, particularly the North-East Monsoon (November—December). It was also the season when the number of respiratory infections as well as other specific fevers of childhood was at its peak. It was the time of year when gastro-intestinal disease was at its nadir.

Summary and Conclusions

Intestinal parasitism was the chief cause of ill health in children in hospital. Ascaris lumbricoides was the commonest intestinal parasite and the Trichuris trichiura was the second. The incidence of intestinal parasitism rose with each year of life and was extremely high at 5 years and over.

Nutritional disorders were common including many cases of fatty liver and oedema as well as of Vitamin A and riboflavin deficiences. A pre-Bitot pigmentation which was often the precursor of a Bitot and a "gutter" pigmentation of the lower part of the sclera are described. The former was a vitamin A deficiency and the latter was probably due to combined vitamin A and riboflavin deficiencies.

Among the respiratory diseases bronchopneumonia caused a high fatality rate in the age group below 5 years.

Gastro-intestinal disorders showed a peak in incidence during the first year of life, the fatality rate was high also in following years. Salmonellosis was a common cause of diarrhoeas in infancy and early childhood.

The vast array of preventable diseases is heartrending. All possible forces and resources of the country should be marshalled and put into action in order to reduce the unnecessary suffering and sorrow caused to children by poverty, superstition, ignorance, wrong food habits and pernicious teaching by those who should know better.

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The Danish Paediatric Society

(Editor: Harald Kreutzfeldt, Copenhagen)

Meeting, January 14, 1953

E. Winge Flensborg: Elisabeth Svensgaard, M.D., deceased 29. XII. 52. An appreciation.

K. Wilken-Jensen (demonstration): A case of zoster.

P. Brændstrup & E. Winge Flensborg: The relation of retrolental fibroplasia to oxygen therapy.

Retrolental fibroplasia was unknown in Denmark before 1949. By systematic examination during the past few years in the Children's Hospital, Martinsvej, Copenhagen, a significant frequency of this condition could be demonstrated and a total of 24 cases was registered to which may be added 7 cases from the department for diseases of the eye, Rigshospitalet, Copenhagen. Out of these children, 8 have become permanently blind and 4 suffer from impaired vision, while the changes in the remaining cases were transient. Several authors abroad, independently of one another, have voiced the opinion, that the condition is related to liberal post-natal oxygen therapy. An analysis of the present material, with the deficiencies which it implies, seems to confirm such a relation and to afford, in addition, suspicion that the oxygen therapy rather than the degree of prematurity is the decisive factor. As cases of fibroplasia without previous oxygen therapy have been recorded, and as only a minority of the children treated with oxygen develop the condition, an individual factor must, however, be present. Cases of retrolental fibroplasia have not been observed *during* the course of oxygen therapy, but frequently a short period after its withdrawal, a fact which may support the presumption that the condition is to be interpreted as a relative anoxaemic retinopathy. From various quarters, such convincing evidence of the principal rôle played by oxygen therapy in the development of fibroplasia has now been produced that it is unquestionably advisable that oxygen be administered on very strict indications, for the shortest possible period and with gradual reduction in the percentage of oxygen.

Discussion: *B. Lindquist*, Lund, reports that in the past 2 years he has only had 3 cases of retrolental fibroplasia out of an annual intake of approximately 100 premature infants. Oxygen is only administered by him to asphyxiated patients, and then, as a rule, only for some days.

Jørgen Pedersen: Blood sugar during the first day of life in infants of diabetic mothers.

The blood sugar curves of 27 infants of diabetic mothers and of 28 infants of non-diabetic mothers were compared. The blood sugar was determined, on an average,

7 times during the first day of life, and the children were kept under standardized conditions including strict diet. 1) The configurations of the blood sugar curves were practically identical during the first day of life in infants of diabetic mothers and of non-diabetic mothers, when the infants were kept under standard conditions. The curves form a more or less undulating plateau. — 2) The level of the undulating curve does not change during the course of the first 24 hours after birth. Infants of diabetic as well as of non-diabetic mothers tolerate hunger and thirst during 24 hours without the blood sugar level falling. — 3) The average blood sugar level during the first day of life is inversely proportional to the average blood sugar level of the mother during the last months of pregnancy and directly proportional to the average blood sugar level at the delivery (mean value during the last half hour before delivery) when this lies within definite limits. — 4) The blood sugar levels of the infants are also proportional to their birth weights: inversely proportional in infants of diabetic mothers and directly proportional in infants of non-diabetic mothers. — 5) As a consequence of the undulating blood sugar level and the correlations found, the average blood sugar in infants varies. Therefore, no generalisations can be made concerning the question whether the blood sugar is lower in infants of diabetic mothers than in those of non-diabetic mothers. — 6) No relation between pathological symptoms during the neonatal period and the blood sugar of the infants could be demonstrated.

Discussion: *Englesson* (Lund) mentioned a number of factors which suggest that the mortality in children of diabetic mothers may be attributed to hypopotassaemia.

J. Vesterdal, K. E. Foght-Nielsen & G. Thomsen: **The results of 214 air-encephalographies in children.**

During the period January 1948—July 1952, air-encephalographies were performed on 214 children suffering from epilepsy, mental deficiency, spasticity, choreic athetosis, ataxia or various combinations of these symptoms, in the paediatric department, Rigshospitalet, Copenhagen. In 62 (the majority epileptics), normal air-encephalograms were found, while in nearly all of the remaining cases, signs of cerebral atrophy of a greater or lesser extent were encountered. There was only slight correlation between the nature of the symptoms and the character of the atrophy, and very frequently there was great disproportion between the degree of severity of the symptoms and that of the atrophy. Patients with hemiplegia or unilateral fits had, as a rule, most pronounced atrophy in the contralateral hemisphere. In 2 cases, agenesis of the corpus callosum was found. In no case were conditions found, suitable for neurosurgical therapy. This is quite understandable as all patients, suspected to be suffering from cerebral tumours, were immediately transferred to the neurosurgical department and air-encephalography was performed there. They are therefore not included in this material.

Discussion: *K. Krabbe, P. Plum, P. Bræstrup.* The participants in the discussion stress that the investigations are of considerable scientific value but of lesser practical significance.

J. Vesterdal: **Nephrosis.**

Nephrosis occurs both as pure lipoid nephrosis and with nephrotic symptoms superimposed (erythrocytes in the urine, raised blood urea or hypertension). Two stages of the same condition seem to be concerned. Recovery may be seen in both forms. The glomeruli are primarily affected, while the changes in the cells of the

tubules are secondary. The oedema is attributed partly to hypo-proteinaemia and partly to hyperfunction of the cells of the tubules (increased resorption of water and salts on account of endocrine disturbances). Infections and treatment with A.C.T.H. or cortisone may occasion excretion of the oedema but recovery is only seldom seen in this connection. To illustrate the prognosis, it is mentioned that out of 5 cases of pure lipoid nephrosis admitted to the paediatric department, Rigshospitalet, 1 recovered, 1 probably recovered, while 3 still had symptoms 9 months—4 years after the commencement of the disease. Out of 8 cases of nephrosis with superimposition of nephritic symptoms, 2 recovered, 2 probably recovered, while 3 still had symptoms 1—2 $^1/_2$ years after the commencement of the disease, while 1 died from intercurrent infection.

Discussion: *P. From-Hansen:* Achieved complete remission in several cases following nitrated mustard gas. He supplies a preliminary account of the results achieved to date.

Meeting, February 11, 1953

Frits Neukirch: **Poliomyelitis. With special reference to the epidemic in 1952—53.**

From 7. VII. 52 to 8.II.53 a total of approximately 2,900 patients with poliomyelitis were admitted to Blegdamshospitalet, Copenhagen, of whom approximately 1,000 were paralytic. Threehundred and forty-one patients had respiratory paralysis and/or paralysis of swallowing to such an extent that special therapy was required. The first 31 patients of this category admitted were treated according to previous principles, i.e. artificial respiration, possibly combined with tracheotomy. Twenty-seven of these cases died (mortality 87 %), a mortality corresponding entirely to that of so-called bulbar poliomyelitis in previous years. Partly on account of the very poor prognosis under the previously administered therapy and partly on account of the exceedingly great number of extremely ill patients in this category admitted, a new method of treatment was introduced from 26.VIII.52 with co-operation between anaesthetists, specialists in diseases of the ear and epidemiologists. The treatment consisted of early tracheotomy, introduction into the trachea of a rubber tube with an inflatable cuff so that it fitted closely to the walls of the trachea and manual positive-pressure ventilation via the tube (usually with a mixture of 50 % oxygen and 50 % nitrogen from a compression cylinder) by means of a rubber bag and a carbon dioxide absorber with soda-lime (a so-called to-and-fro system). By frequent suction through a cathether introduced through the tracheal tube, it is possible to maintain the airway free from secretion and by the above form of artificial respiration it is possible to ventilate the patients adequately.

The results of treatment of the 310 patients (as treated until 5.II.53) appears from the Table. By this method, a reduction in the mortality to 38 % was achieved. For the first 50 patients treated in this way, the mortality was 54 % and for the last 50 patients it was 22 %. As regards the condition of the patients otherwise, it should be stated that the 48 patients discharged have no paralyses of the extremities or practically none. Of the 103 patients who are still in hospital and who can breathe spontaneously, the majority have slight to moderate paralyses, a minority have severe paralyses and the 43 patients who still receive artificial respiration have very severe paralyses: approximately half of them, 3—5 months after the commencement of the disease, are practically completely paretic in all extremities. By the method described, a reduction in the mortality of patients with paralysis of respiration or

TABLE 1

Patients with Paralysis of Respiration and/or Paralysis of Swallowing.

Total	Men 84	Women 69	Children 157	Total 310
Dead	41	21	54	116
Artificial respiration still	15	14	14	43
Spontaneous respiration + endotracheal tube	10	6	18	34
Spontaneous respiration, endotracheal tube removed (or no tracheotomy)	12	17	40	69
Discharged	6	11	31	48

paralysis of swallowing or both has been achieved from approximately 80 % to approximately 40 %.

Discussion: *J. Vesterdal:* Accounted for a small epidemic in November—December 1952 in the paediatric department, Rigshospitalet, Copenhagen, of lymphocytic meningitis among infants. A total of 9 cases was concerned. The meningitis was very mild. Four cases had approximately only 20 cells/cmm. in the cerebro-spinal fluid, 4 had 2—5 cells/cmm. but completely resembled the former cases clinically and 1 case had 71 cells/cmm. Isolated cases only had pyrexia. The fontanel was tense for a week and during this week the infants did not thrive. Thereafter, the condition disappeared without sequelae. No case developed paresis. The incubation period must have been approximately 1 week. Simultaneously with this epidemic, several of the nurses had slight symptoms resembling influenza which lasted for one day, accompanied in some with pain in the nuchal region. This was probably the same condition. — *A. Rothe-Meyer:* Asked about the incidence of cases of relapse (infection with another virus type). Is vaccine available against one or several types? — *C. Friderichsen:* Asked the age of the youngest and oldest cases of poliomyelitis, seen in Blegdamshospitalet. Mentioned a newly-born infant, who at the age of 5 days developed a total flaccid paralysis of both upper and lower limbs and also of the pelvic musculature. No case in the patient's environment. At the age of 3 months, the infant was nearly completely paretic, without, however, bulbar symptoms. — *F. Neukirch:* Was convinced that aparalytic poliomyelitis was concerned in the material presented by Dr. Vesterdal, this being also in good agreement with the incubation periods. Had observed several cases in the epidemic of poliomyelitis concerned where, in all probability, the patients had had poliomyelitis twice. A child, admitted in August—September 1952 with aparalytic poliomyelitis, was readmitted approximately 3 weeks later with paralysis of respiration. Unfortunately, virological and serological examinations were undertaken only in a minority of the patients, so that absolute certainty, whether poliomyelitis, caused by different types of virus was concerned, could not be obtained. The vaccine, now prepared in U.S.A., contains dead viruses of all three known virus types. The youngest patient with paralytic poliomyelitis was 12 days old and the oldest 70 years. He was not aware of any definitely proved intra-uterine transfer of infection to the foetus so that a child would be born with poliomyelitic paralysis. The child

which Dr. Friderichsen mentioned, which developed poliomyelitis with paralyses at the age of 5 days, may well have been infected at birth if the mother was a virus carrier.

Esther Frantzen and Mogens Bjørneboe: **Acute non-diphteritic laryngitis at Blegdamhospitalet. — A comparison between the symptomatology of the disease in 1941—42 and in 1951.**

The object was to investigate if the disease, according to the impression which has been received, has during the course of years changed character and has become a serious disease. The two groups of patients comprise 158 and 300 patients respectively. The duration of the disease was calculated, the condition on admission, the course of the disease during the stay in hospital, the frequency of complications and the results of laryngoscopical examination and treatment. It appears from the investigation that the cases from 1951 were somewhat more severe than were the cases from 1941—42. The mortality was, however, greater in 1941—42 than in 1951 (3.8 % and 1.7 %). The explanation is probably that the treatment now is more effective. Tracheotomy is employed more frequently (12 cases as opposed to 2 cases) and antibiotic treatment has been introduced. A gradual transition exists between the cases which take a mild course and the severe cases of the disease and it does not seem to be possible to establish a definite prognosis at an early stage of the disease.

Mogens Bjørneboe, Esther Frantzen, H. Poulsen and Kirsten Rosendal: **A bacteriological investigation of acute laryngitis in children.**

Bacteriological examination in 39 children with primary acute laryngitis was carried out. Swabs were taken from the larynx by direct laryngoscopy. Microscopical examination and culture were undertaken in Statens Seruminstitut. In addition, swabs from the larynx were taken in 9 control individuals. In the patients with laryngitis, a long series of pathogenic and non-pathogenic bacteria was found. The bacterial flora did not, however, deviate from that found in the control individuals. On culture from the blood in the same patients, growth was obtained in 1 case only, viz. Pfeiffer's bacillus (type B) which was simultaneously demonstrated in the larynx.

Discussion: *I. Falbe-Hansen* stressed that although acute laryngitis has a favourable prognosis, the prognosis in cases with descending infection is still very serious. Accounted for 24 cases of acute stenosing laryngo-tracheo-bronchitis which may be arranged in the following groups: Subglottal laryngitis without descending infection (so-called pseudo-croup): 3 cases; with descending infection: 10 cases. — Supraglottal laryngitis without descending infection: 5 cases; with descending infection: 6 cases. — All cases underwent tracheotomy. The mortality was 37 %. Eight children were one year or less and of these, 5 died; 16 were over one year and of these, 4 died (62 % and 24 % respectively). The situation and the extent of the condition is decisive for the prognosis. Out of 10 children with subglottal laryngitis with descending infection, 9 thus died, while in the remaining groups, no fatal cases occurred. Out of the 7 patients who underwent bronchoscopy, 4 died. Three recovered after 1—15 bronchoscopies. Early tracheotomy under anaesthesia is advocated following intubation and suction together with energetic medical treatment. — *C. Friderichsen:* Vigorously criticised the fact that the lecturer classified laryngitis stridula and fulminating laryngo-tracheo-bronchitis together in one group, maintaining that they are two different diseases with different

clinical pictures and with only the stridor in common. He described the clinical and pathological anatomy of fulminating laryngo-tracheo-bronchitis and emphasized the difficulty in the differential diagnosis from pseudo-croup, capillary bronchitis and acute infectious atelectasis. He was of opinion that a great number of the severe cases, presented under the diagnosis of pseudo-croup, were cases of fulminating tracheo-bronchitis. He pointed out, that information on results of autopsies, particularly as regards atelectasis, was lacking. — *M. Bjørneboe:* Maintained that he and his co-workers were of the opinion that a definite prognosis cannot be established at the commencement of the disease. The diagnosis of pneumonia in their material implied both pneumonia and atelectasis and the latter diagnosis was only established in the material from 1951. A special type of laryngitis, caused by Pfeiffer's bacillus (type B) with supraglottal oedema, which is mentioned in the literature on several occasions, could not be distinguished in their material.

Meeting, March 2, 1953

Henning Andersen, G. Asboe-Hansen and Flemming Quaade: **Biopsy of the skin in the diagnosis of myxoedema in children.**

Using the technics described by Asboe-Hansen (Thesis, Copenhagen 1951), an attempt has been made to evaluate this method, mainly based upon the amount and distributions of mucopolysaccharides and mastcells in the corium, in the diagnosis of myxoedema in children. The histological diagnosis has been made by A-H, while the clinical diagnosis of myxoedema was made by H. A. and F. Q. The two evaluations were undertaken independently of one another and the results were not compared until later. Results:

23 children with definite myxoedema: 14 positive, 9 negative skinbiopsies.

24 children more or less suspected of having myxoedema: 10 positive, 14 negative skinbiopsies.

36 euthyroid children: all negative skinbiopsies.

In children with positive biopsies, the changes in the skin could be demonstrated to follow the withdrawal respectively the administration of thyroid. The causes of negative biopsies in children with myxoedema are discussed. Emphasis is laid upon previous investigations indicating that thyrotrophic hormone might be responsible for the accumulation of mucopolysaccharides etc. in myxoedema. If this is the case, negative biopsies must be anticipated in cases of myxoedema of hypophyseal origin. It has not yet been possible to divide the material satisfactorily into myxoedema of hypophyseal and of thyroid origin. Another cause of negative biopsies in children already under treatment might be a too short withdrawal of thyroid. A period of 6 weeks without medicamentation seems to be necessary in those cases. Conclusions: Skin biopsy, an easy and rapid method, seems to give strong evidence of myxoedema if positive. Negative skin biopsy does not exclude myxoedema.

Discussion: *J. Vesterdal:* What happens if cortisone is administered to patients with myxoedema? — *G. Asboe-Hansen:* In one case, where this was attempted, nearly all the mucin disappeared from the tissues. — *C. Friderichsen:* Can these tests be employed for myxoedema in adults? — *A. Rothe-Meyer:* How long must thyroid be withdrawn before the changes are manifest again? What is the minimum age at which changes in the skin have been demonstrated? — *Henning Andersen:* We know nothing of the changes in senile myxoedema. — The rates of appearance

and disappearance of the changes probably depend to a great extent on the dosage of thyroid, perhaps also on other factors. In the present material, a period of 3—6 weeks is concerned. The changes seem to develop early in the condition. The youngest child with myxoedema on whom I performed biopsy was 3 months of age. The biopsy was positive. This child is, however, not included in this material which originates from Johns Hopkin's Hospital, and the case was not evaluated by Asboe-Hansen.

Ole Mortensen: **A case of galactosaemia with amino-aciduria.**

Galactosaemia is a congenital familial condition, which manifests itself by reduced or absent ability to metabolise galactose in the normal way. The symptoms consist of failure to grow and thrive, impaired motoric and mental development, cataract, enlargement of the liver, galactosaemia, galactosuria and albuminuria. Pyrexia, dyspeptic symptoms and osteoporosis are frequently encountered and, in a number of cases, there is marked jaundice during the first days or weeks. The treatment consists of milk-free diet.

Case history: (The paediatric department, Aarhus Municipal Hospital, case-history No 153/53). In a girl aged 5 months, typical symptoms of galactosaemia were encountered. The diagnosis was established by chemical and paper-chromatographic demonstration of galactose in the urine (Sv. Darling, Ph.D.), by galactose tolerance test and by the clinical improvement of the condition on a milk-free diet. The cerebro-spinal fluid showed increased protein content. Calcium in increased quantities and amino acids in considerable quantities were excreted in the urine. On treatment with a milk-free diet, galactose and albumen disappeared from the urine, the excretion of calcium and amino acids diminished considerably and the cerebro-spinal fluid became normal.

Discussion: *Oluf Andersen:* Were changes in the reflexes or other neurological symptoms demonstrated? — *P. Bræstrup:* What is known concerning the effect of insulin? — *Ole Mortensen:* The deep reflexes were present throughout nor were any other neurological symptoms encountered. Insulin could produce hypoglycaemic attacks in the patient in question. Galactose can hardly substitute glucose in the central nervous system.

Ib Boesen and Tage Samsøe-Jensen: **Acute dyspepsia in bottle-fed infants under the age of 7 months treated with penicillin intramuscularly and dihydrostreptomycin orally.**

During 2 years 117 infants suffering from acute dyspepsia (= acute gastro-intestinal disease requiring dietetic treatment but without intoxication or signs of acidosis) have been treated in two groups so that half of them were given carrot-powder-soup and a gradual supplement of milk — and the other half Darrow's solution mixed with 5 % aqueous glucose solution (1 + 2) for 12 hours and thereafter milk and water mixture increasing after 24—48 hours to the normal diet for the age of the child. Simultaneously the other group of infants for five days were given 100000 units procaine-penicillin intramuscularly daily and dihydrostreptomycin orally approximately 100 mg. pr. kg. body weight pr. day. No difference was found in the frequency of defaecation during and after treatment within the first 12 days, and all infants increased satisfactorily in weight after the conclusion of the treatment, but the period

of treatment was shorter in the latter mentioned group which were given antibiotic treatment.

Discussion: *M. Nathan:* May antibiotics be employed to such an extent as was the case here without apprehension? — *Oluf Andersen:* Cases with dyspepsia of parenteral origin were not separated in the material; they are frequently of shorter duration and particularly susceptible to antibiotics. Dyspepsia in institutions takes a course different from that found in a material of out-patients. He warned against extensive employment of streptomycin. — *E. Flensborg:* Felt no apprehensions in employing antibiotics. Only 5 % of streptomycin is absorbed when administered orally. Was unable to decide when dyspepsia was of parenteral origin. — *P. Bræstrup:* Employed a dietetic régime leading to a normal diet for the infants in the course of 8 days. — *A. Rothe-Meyer:* Was of the opinion that the time saved (2 days) was not sufficiently conspicuous to justify the employment of the treatment. — *E. Gjørup:* Stressed the essential significance of the mental condition of the infants concerning the duration of the disease.

Sv. Brandt: **Congenital polyporous encephalopathy.**

A newly born, full-term infant was admitted to hospital on account of failure of temperature regulation, feeble crying and frequent generalized twitchings. Encephalography performed on the 7th and 41st days of life revealed completely abolished activity. The cranium appeared to be pellucid and puncture of both hemispheres via the coronal suture together with suboccipital punctures followed by substitution of the fluid by air, showed extensive cavitation on X-ray examination, localized to the white substance of the hemispheres, traversed by trabeculae and not communicating with the ventricular system, the protein content of which was normal while the fluid of the cysts was very rich in protein and slightly xanthochromatic. With the object of inducing delivery, the mother had received a) about 4 weeks before the delivery, approximately 240 drops extractum fluidum secalis cornuti (liquid extract of ergot, Pharmacopoea Danica, 1948) 3 times daily for 10 days (i.e. nearly 5 times the maximal dose), b) 3 weeks prior to the delivery, 4 g quinine in the course of 2 days, c) for 4 months prior to the delivery, 45 drops of morphine daily (corresponding to approximately 1.25 g of a 2 % solution of morphine hydrochloride).

Meeting, April 22, 1953

A. Biering (demonstration): **Cutis hyperelastica s. laxa (Ehlers-Danlos) manifest by subcutaneous haemorrhages and slightly prolonged coagulation time.**

Bent Friis Hansen: **Case of "agnogenic myeloid metaplasia".**

The child, a boy aged $2\,^{10}/_{12}$ years, was admitted to the department 6 months previously for observation for leucaemia with acute haemorrhagic diathesis. On admission, marked enlargement of the liver and spleen, slight anaemia, 65000 leucocytes and 20000 thrombocytes per cm were found. The differential count showed 2—4 % blasts but was otherwise normal. The bone marrow was cellular and contained 13 % blasts. His condition deteriorated during the following months, the leucocyte count rising on one occasion to over 200000 cells/cmm still with only few immature cells,

the thrombocytes fell to 2000 and the child developed a haemolytic crisis with pyrexia, rapid fall in haemoglobin and reticulocytosis of over 100 ‰. Splenectomy was therefore undertaken. The patient tolerated the operation well but no noteworthy improvement in his condition occurred, apart from that attributable to the transfusions in connection with the operation. Ten days after the operation, further transfusions were required on account of persistent haemorrhage from the nose and mouth.

Svend Helbo: **Oral penicillin as prophylaxis against streptococcal infections in a children's institution.**

An account was given of treatment with 200000 units of penicillin orally daily to 168 children, who were treated for a total of $4\,^1/_2$ months. As a control material, 178 children were treated with dummy tablets. There were no bacterial carriers and no streptococcal infections in the group of children treated with penicillin and the morbidity on account of other nosocomial infections was less, as secondary streptococcal infections were avoided. There were no side-effects attributable to the treatment and no penicillin-resistant strains of streptococci developed.

Discussion: *Vesterdal:* Prophylaxis not only against streptococcal but also against staphylococcal infections is important. *Flamand-Christensen* maintained that patients with nephritis and others who were particularly exposed to streptococcal infections in an institution should be treated. — *Biering-Sørensen* doubted if an adequately high concentration in the blood could be obtained by oral treatment with penicillin. — *A. Rothe-Meyer* wanted examples of intermittent treatment of personnel in institutions and to know the results of systematic treatment at the commencement of the children's stay in hospital.

P. Plum: **Cinematographic demonstration of spastic children.**

In conjunction with the film, an account of the principles of treatment, the method of treatment and the results were given. The significance of early diagnosis and treatment, preferably in the first year of life, was emphasized and further, the advantage of instructing the parents and educating them in the treatment so that this could be undertaken in the home. In addition, apparatus was demonstrated, both special orthopaedic apparatus and simple technical aids which the parents themselves could make.

Meeting, May 4, 1953

Thamdrup **(demonstration): Monstrous encephalocele.**

J. Vesterdal **(demonstration): Monstrous encephalocele.**

Ib Boesen: **Housing conditions and morbidity.**

Vagn Christensen: **Housing conditions and morbidity.**

A material consisting of 1365 (the total) cases admitted to the Children's Hospital, Martinsvej, Copenhagen, in 1950 was presented. Forty-two cases were excluded on account of insufficient information while 106 were re-admissions. The number of

rooms in the flats from which the remainder, 1204 cases, originated, was compared with the average number of rooms in flats in Copenhagen, occupied by families with children. More frequent, and statistically significant admissions were found from 1-roomed flats and from flats with many children. More frequent admission seemed to show a maximum in the first 2 years of life. Investigation of the diseases chiefly responsible for frequent admission showed that respiratory diseases, gastro-intestinal diseases and rickets were mainly concerned while the number of admissions due to "neuroses", enuresis and encopresis were less preponderant in children from poor housing conditions. — A number of uncertain factors in the investigation were pointed out and a further investigation in which elimination of these factors has been attempted was mentioned.

Harriet Holst and Vagn Christensen: Housing conditions and morbidity.

By visiting 89 families in their homes, partly flats in slum courts in Vesterbro and partly in a district with terrace-houses as a comparative material, greatly increased frequency of admission to hospital of children under 7 years was found in the material from Vesterbro. These admissions comprised mainly respiratory and gastro-intestinal diseases. In addition, in Vesterbro, there was much greater morbidity treated at home and many more frequent complaints of nervous conditions in the children. The excess costs for hospitalization and convalescence amount to 240 Danish crowns annually per family for the children alone.

Erik Thamdrup, E. Winge Flensborg and Troels Smith: Housing conditions and rickets.

Material from the paediatric departments in Greater Copenhagen in 1946—1951 inclusive. Based upon a material comprising 396 cases of definite rickets in children of under 1 year from the Municipality of Copenhagen, a map has been prepared, showing the relative frequency of rickets in the various districts of Copenhagen. Distinct preponderance was demonstrated in quarters with particularly poor housing conditions (2—7 times the average frequency). As causes of this are mentioned, 1) that these quarters in particular lack adequate daylight, 2) that poor housing conditions exert a dulling influence upon the parents so that the care of the children deteriorates.

Discussion: *Heinild* stressed that the relation between housing and disease must not be conceived purely mechanically as there are many differences between living in a 1-roomed flat and living in a 4-roomed flat other than the purely spatial difference. — *Biering-Sørensen:* The frequency of admission is not the same as the morbidity, as the quality of the housing plays a rôle here. Suggested that health visitors and school-authorities were asked for cooperation in future investigations in this field. — *Munkvad* was not of the opinion that the population in slum quarters is constitutionally inferior. A condition of "social dementia" is probably concerned and this is the final stage of the many stresses to which these individuals have been exposed and from which they have difficulty in falling themselves. — In replying to points raised in the discussion, *Vagn Christensen* stated that more frequent admission to hospital probably corresponds approximately to a greater morbidity. This is supported both by an impression of the hospital material, calculation of the average number of days of illness and investigations based upon home visits. More neuroses probably

exist among children in poor environmental conditions but it is conceivable that they are of another type, less marked by competition than in children living under good environmental conditions.

Folke Tudvad: **Impressions from U. S. A.**

The investigations routinely undertaken in children with renal diseases in the large departments in U.S.A. and the significance of some of these investigations together with the treatment of renal diseases, particularly the nephroses, were mentioned. The Societies for Nephrotics were mentioned. Some theories and facts concerning the development of oedema and the mode of action of cortisone and A.C.T.H. were reviewed. Finally, the part played by the kidneys in the regulation of the acid-base equilibrium and the effect of the carboanhydrase inhibiting substance 6063 (Diamox) was mentioned.

Meeting, June 10, 1953

O. Steinicke-Nielsen: **Congenital pyloric stenosis as a predisposing factor in the ulcer syndrome.**

The etiology of pyloric stenosis was mentioned, and the question was shortly reviewed as to what extent the pyloric hypertrophy persists after the cessation of the acute symptoms in the infant and if there was reason to suppose that pyloric stenosis in adults is a direct sequel of the congenital type, which did not seem to be the case. In order to determine if gastric ulceration and gastritis develop more frequently in individuals with previous congenital pyloric stenosis than in others, 95 individuals (73 males and 22 females in the ages 25 to 45 years) were questioned. All of these were treated medically in children's hospitals in infancy for congenital pyloric stenosis. The object of the investigation was to obtain information about the present and previous conditions of these individuals, particularly concerning possible dyspeptic complaints. As a control group, 100 patients, selected at random, from a hospital material (77 males and 23 females in the ages of 25 to 51 years) were questioned. In the basic material, 28 per cent, were found to have more severe dyspeptic complaints as opposed to 12 per cent in the control group. The investigation shows that adults with previous congenital pyloric stenosis show a greater frequency of dyspeptic conditions (gastritis and gastric ulceration) than do the control group. In addition, the investigation shows a significantly more frequent occurrence of gastritis and gastric ulcer among the parents and siblings of those questioned in the basic material than in the control material.

O. Steinicke-Nielsen: **Familial predisposition to congenital pyloric stenosis.**

With the same basic materials as in the above mentioned work, the patients were questioned concerning possible familial occurrence of congenital pyloric stenosis. — Among 128 children of 63 probands (32 had no children) with previous pyloric stenosis, a total of 11 cases were found with congenital pyloric stenosis. In the control material 68 probands with a total of 145 children were present (32 had no children), and of these one had congenital pyloric stenosis. Among a total of 216 siblings of the indi-

viduals who previously had suffered from congenital pyloric stenosis, 9 cases of pyloric stenosis were found. In the control material, among 319 siblings, no known cases of congenital pyloric stenosis were found. In addition, 8 cases of congenital pyloric stenosis were found among the other members of the families of the basic material as opposed to one case in the control group. In comparison with previous works concerning the frequency of congenital pyloric stenosis in a normal population, the investigation showed a significant familial preponderance of the condition.

Discussion: *Flamand Christensen:* May not pyloric stenosis be interpreted as a link in a "stomach-complex", found in these families, rather than a predisposing factor to the ulcer syndrome? — *S. Brandt* raised the same question in asking if it were not a question of constitution. — *P. Plum:* Expressed doubt whether the difference between the control material and the basic material in the first investigation actually is significant. — *O. Steinicke-Nielsen:* It cannot be excluded that the constitution may play a rôle; mentions, however, that many individuals of pyknic type were present in the material. The difference, in any case purely numerically, is statistically significant.

F. Tudvad, H. McNamara, and H. Barnett: **The excretion of bicarbonate and potassium in premature infants.**

The investigations mentioned were undertaken to answer the following questions: 1) Does the immature renal function of the premature infant play any part in its "physiological" acidosis? 2) Can this acidosis be corrected by bicarbonate? 3) Are premature infants capable of excreting potassium as satisfactorily as adults? Investigations were undertaken on 12 premature infants following intravenous injection of bicarbonate alone or combined with a single intravenous injection of the carboanhydrase inhibiting substance 6063, and also a combination of these two procedures and intravenous infusion of potassium chloride. The investigations showed: 1) Premature infants do not have a lower tubular resorption of bicarbonate than have adults, and this part of the renal function will, therefore, tend to maintain the serum bicarbonate concentration at about 24—25 mEq/litre. Acidosis in premature infants must therefore be attributed to other causes. 2) It is possible to raise the serum bicarbonate in premature infants by administration of bicarbonate, and finally 3) The tubuli in premature infants, as in adults, are actively capable of excreting potassium and the immature renal function of premature infants, therefore, gives no cause for further reduction in the rate with which potassium containing fluids are administered.

Discussion: *P. Bræstrup:* Asks the weight of the premature infants. — *Tudvad:* The weights of the infants were between 1700 and 2200 gm. Questioned by *Gjørup*, whether the premature infants were not better off with their low HCO_3 values, Tudvad answered that it had not been demonstrated that HCO_3 values are injurious and therefore it is not always necessary to relieve the acidosis.

A. Rothe-Meyer: **Points of view on paediatric reform.**

A number of factors which inhibit the work and possibilities of development of Danish paediatrics were brought forward for discussion. The present medical staffing of children's hospitals is quite adequate to undertake the clinical treatment of the patients, but is unsuitable for solving two other indispensable tasks: *Medical education*

and *scientific research*. Housephysicians during their brief, changing appointments, cannot extend interest to more than the clinical routine work and their continued careers. Registrars may produce scientific work simultaneously with working up a practice as a means of existence. The chances of obtaining a position as physician-in-charge are small and the fear of missing contact with the active front line of paediatrics after the conclusion of training, is an increasingly heavy burden during the period as registrar. Finally, the physician-in-charge is often so occupied with administrative and semi-official duties that he cannot maintain scientific continuity in his department. The future medical staffing in the leading paediatric departments should include 3 different groups of subordinate and medical appointments.

1) A *clinical group* consisting of registrars and house physicians with periods of employment of 3 years and 1 year respectively. In addition, there should be a certain number of short-term appointments (e. g. 3 months) for physicians from other medical specialities who want some paediatric education. These latter appointments should not be regarded as constituting the normal qualified staffing.

2) A greater or lesser group of physicians, who are mainly occupied with *paediatric research* and who may hold these positions for 1 to 3 years.

3) A group of more *loosely attached specialists* in paediatrics and allied specialities, who are employed part time as co-workers in the wards, out-patient departments or special clinics. This group makes it possible inter al. to utilize paediatric specialists, who after the conclusion of their clinical training have been forced to go into practice but who, for clinical or scientific purposes desire continued connection with hospital work.

To lead and co-ordinate the clinical, educational and research work it is necessary to appoint a *permanent physician-in-charge and a permanent assistant.*

The *children's hospitals* should comprise a link in the chain of central hospitals. They should be equipped with an ample number of isolation rooms or, preferably, an entire ward of them. Finally, they should be equipped with outpatient departments where both the further clinical and scientific specialization of paediatrics may take place. Not only in Copenhagen, but also in a number of provincial towns, children's departments are required which can cover the functions mentioned here. A more far reaching future scheme lies in letting these hospital out-patient departments develop into *centres for child health*, where, in addition, the prophylactic requirements for health in childhood are undertaken.

Discussion: Among the participants in the discussion, there was, to a great extent, approval of the points of view set forth. The necessity of acknowledging scientific work as a normal part of the function of the ward was stressed. (*P. Bræstrup.*) *P. Plum* mentioned that many institutions which deal with children, deaf, blind or handicapped in other ways, lack paediatric assistance. — *A. Rothe-Meyer* proposed that other members work out proposals and that the question be taken up for discussion later.

Proceedings of the Section for Pediatrics and School Hygiene of the Swedish Medical Society

Meeting, March 20, 1953

de Rudder (guest. by invitation): Poliomyelitic problems.

The late summer peak in the seasonal curve of poliomyelitis is still unexplained. It has no connection with the curves of precipitation nor temperature. Geographical investigations of polio-epidemics show that the disease is more common in Northern than Southern countries. A local epidemic does not spread according to rule as do other infectious diseases. Contrary to other infections polio has continuously shifted towards higher ages. Also the type of syndrome has changed, uncharacteristic forms now being much more frequent than before.

E. Hagberg and *B. Johannsson:* Micrognathia with lingual obstruction of the pharynx.

Report of a case successfully operated on, according to a minor modification of the method of *Douglas*.

A. Dahlström and *H. Gladnikoff:* Cases of leukemic blood pictures.

I. Alm: Differences in the mortality of single and multiple premature births.

From a follow-up study of the social prognosis of legitimate male prematures during the years 1902—21 (Acta Pædiat. 42. Supplement 94, 1953), it soon became obvious that the multiple births should be accounted for separately. They differ in essential respects from the single births. Particularly striking was the fact that the multiple births displayed a substantially higher mortality than the single births. This applied to the total mortality from the whole period of observation up to 1948, as well as to the mortality in infectious diseases. In both instances, the differences were statistically probable. In comparisons between different weight groups also, the mortality of the multiple births kept higher throughout, disclosing rather a tendency to increase with a higher weight at birth, as compared to the single births. The differences in mortality were most pronounced in the first months of life. The differences were not equalized before the age of three years. A tendency to a lower mortality is perceptible for the premature multiple births above the age of 5 years, though it is not statistically significant. The causes of these differences may be a matter of opinion and may, conceivably, be due to an excess mortality of the single births at the Maternal Hospital, though this is not very likely. On the other hand, mothers of twins are often older than mothers of single children. In the present investigation, the age difference between the mothers is statistically significant, in the 2 premature groups. The older mothers are less often uniparous. Therefore comparatively the multiple births more often refer to lat-comers among a number of brothers and sisters. For this reason, an investigation was initiated regarding the mortality of single children and those with older brothers or sisters. The mortality was then found to be higher in the case of late-comers. The difference was statistically significant in the control group of full-term infants, statistically probable among the single births and probable, though not proved, among the premature multiple births. In a larger series, the difference would, however, very likely prove to be significant. Thus, in a selected, socially and economically uniform, series, belonging to Social Group III, which includes those

with the lowest earnings, a statistically significant difference was obtained between premature single births and premature multiple births. In all probablility, this increase in mortality depends on an excess mortality from infectious diseases during the first 2—3 years of life. Partly, the explanation may be found in a late order of birth and a greater number of older brothers or sisters. A contributory factor may be that, in Social Group III, the less well circumstanced people have the largest number of offspring, with a consequently bigger likelihood of having twins. Contrariwise, in similarly selected series from the years of 1944—1946, the multiple births will be found to thrive better than the single births up to 1 year of age. This agrees with observations in the literature. The reasons are, probably, that deaths from infections have become rare also among prematures, and, in addition, that improvements have taken place in the social conditions. A contributory factor may be found in the fact that the frequency of multiple births has been steadily falling, even during the rise in the number of births recorded in the forties. The children born and multiple births that occur nowadays, seldom refer to those born after the second or third child.

B. Werner: Cases of hepatocerebral degeneration in infants.

These cases were unusual in so far as they concerned newborns. The disease had an acute course and death occurred before the lapse of four months. They were children of the same parents, born at an interval of 2 years. The parents were in good health and had no blood relationship and the heredity was good. The parents had two children, a few years older. A brother born between these two had died at the age of three months with a set of symptoms similar to that of the present two cases. The infants were both fully developed. At birth, their condition was normal. A slight dysphagia was already present at the Maternity Hospital. In one of the two cases, it afterwards became pronounced. From a fortnight old, both had remittent pyrexia. In their febrile state, the patients lay, strongly hypertonic, with trunk stretched and head bent back. During the afebrile periods, an extreme hypotonia was noted in the first case and, in the second, a moderate hypertonia connected with a certain amount of rigidity. In both instances, the liver was, to begin with, slightly enlarged, but increased rapidly in size towards the end of the period of the disease. The patients died with icterus and edema in connection with terminal hepatic enlargement. The laboratory investigations disclosed nothing of particular interest. Patho-anatomical examination: In the case with the pronounced hypotonia cerebral changes were observed, localized principally to the area of the dentate nucleus of the cerebellum. The case in which a rigidity was found, in addition to a hypotonia, the biggest changes were noted in the lenticular nucleus. In both cases, the changes consisted in a loss of nerve cells and an increase of, and qualitative change in, the glial cells, in accordance with the *syndrome of Wilson's disease.* The liver showed, in both instances, pronounced cirrhosis.

E. Hagberg: Toxoplasmin studies.

The author has in collaboration with GARD and MAGNUSSON during November 1950 and February 1951 toxoplasmin tested 430 school children (232 boys and 198 girls).

For the whole age group of 7—14 years, positivity amounts to 14 per cent. No sex difference has been noted. 13.8 per cent of the boys are positive, 14.2 per cent of the girls.

Age	Number	Toxoplasmin positive	
		Number	Per cent
7— 8 år	114	10	8.8
9—10 »	174	26	14.9
11—12 »	99	16	16.2
13—14 »	43	8	18.6

S. Gard: **Comparison between toxoplasmosis and poliomyelitis.**

As far as the latter disease is concerned, the study of its "social serology" (JOHN R. PAUL) has, in a decisive way, contributed to a solution of many difficult epidemiologic problems. The age distribution of the serologic immunity has been found to follow a definite pattern (TURNER and others). Three factors determine the appearance of the age distribution curve, as follows: (1) A transplacental passage of antibodies from mother to fetus and the relatively rapid disappearance (within 3—6 months) of this inherited passive immunity; (2) The gradual development of an active immunity, resulting from exposure to a virus with its concomitant, chiefly subclinical, infections; (3) The limited duration of the active immunity, in so far as it is not maintained by reinfections. When the risk of infection keeps fairly constant, the immunity level will adjust itself to a certain equilibrium in which the annual addition of immune individuals will be found to be in a state of balance with such a number of previously immune cases as are again successively losing their immunity. The average risk of infection can be calculated from the form of the curve of age distribution. An average annual infection risk of about 10 per cent corresponds to an immunity level of 70 per cent in adults, such as prevails in this country. The explanation of the epidemiologic character of poliomyelitis is to be found in the fact that the risk of an invasion of the nervous system and a clinical manifestation of an infection in a not immune individual obviously increases with age. Accordingly, when the average risk of exposure diminishes, and, consequently, the general immunity level is reduced, a growing proportion of those in the higher age group will find themselves in the danger zone. The result will be an absolute increase of morbidity, with the point of gravity deviating towards older and older age groups, notwithstanding a decrease in the risk of infection. Thus, poliomyelitis assumes the character of a civilization disease: the increased medical significance of the infection originating in improved hygienic conditions.

Toxoplasmosis and poliomyelitis have many features in common. The infection is also in the case of toxoplasmosis widely spread and mostly takes a subclinical course. Further, there is reason to suspect that clinical manifestations are more common in old than young individuals, apart, of course, from the intra-uterine infections which present quite a specific problem. It is, therefore, not unreasonable to ask the following question: Is toxoplasmosis also a civilization disease, destined to become of a greater medical significance as the infection becomes less frequent? Such a possibility is sufficiently alarming to justify serious efforts to ascertain the epidemiology of toxoplasmosis. Thus, a study of its "social serology" is in the first place called for. It is from that point of view that Dr. Hagberg's work, now published, has its obvious value. It must, however, be supplemented by similar investigations in other parts of the country. Comparison must be performed between areas differing in density of population and type of habitation, between different social groups, etc. Such data regarding

the frequency of infection as are obtained in that way will in turn throw light on the mechanism of the infection.

E. Hofman-Bang: **Epidermolysis bullosa. Report of a case.**

Meeting, April 10, 1953.

N. Malmberg: **Some comments on the stipulated duty to report epidemic dyspepsia in infants.**

Eric Jacobsson: **The prognosis in cholera infantum with and without aureomycin therapy.**

From a perusal of cases of cholera infantum for the past 6 years at the Children's Hospital Samariten in Stockholm, it emerges that the prognosis for these grave cases of dyspepsia has changed very considerably by the fact that, during the past three years, aureomycin has been applied to all complicated and severe cases of dyspepsia. The risk of a dyspeptic case being aggravated and turning into a cholera infantum syndrome has been greatly reduced. In cases with a syndrome of cholera infantum admitted at the hospital and at once treated with aureomycin, the risk of a fatal issue, though not entirely eliminated, seems to be considerably diminished. It is, however, necessary that other therapy, such as the supply of fluid, neutralization of acidosis, protein and salt administration, etc., is applied adequately and in a way conforming to the precepts of experience.

(To be published in Sv. Läkartidningen.)

T. Johnsson: **Epidemiologic and immunologic aspects of epidemic myalgia.**

In about 50 per cent of 20 hospitalized patients, examined for the occurrence of Coxsackie virus, an etiologic connection has been rendered probable, either by the finding of virus, type B 3, or through a neutralization test. In one instance, a double infection has, in all likelihood, occurred with an A strain, in addition to the aforementioned B strain. A familial occurrence of Coxsackie virus is noted in 3 children with aseptic meningitis, two of them lacking objective symptoms of meningitis. Minor's disease occurred frequently in this epidemic which, like those earlier described, often affected different members of a family. Further support for a supposed etiologic connection between the isolated B type and epidemic myalgia was derived from a neutralization test with pooled sera, one group of affected and various groups of unaffected, people in the locality struck by the epidemic being compared with one another, as well as with an island population among which, at the time, no cases of epidemic myalgia had appeared. In the smaller of the two affected towns, the infection had, apparently, been mainly limited to some minor areas.

BOOK REVIEW

Jules R. Dreyfus: **Säuglings- und Kleinkindpraxis für Nichtspezialisten.** Verlag Paul Haupt, Bern, Schweiz. Preis SFr. 6: 25.